10/ 023,099

```
 NEWS 45  Jun 25  HSDB has been reloaded

 NEWS EXPRESS  April 4 CURRENT WINDOWS VERSION IS V6.01a, CURRENT
               MACINTOSH VERSION IS V6.0b(ENG) AND V6.0Jb(JP),
               AND CURRENT DISCOVER FILE IS DATED 01 APRIL 2003
 NEWS HOURS    STN Operating Hours Plus Help Desk Availability
 NEWS INTER    General Internet Information
 NEWS LOGIN    Welcome Banner and News Items
 NEWS PHONE    Direct Dial and Telecommunication Network Access to STN
 NEWS WWW      CAS World Wide Web Site (general information)

Enter NEWS followed by the item number or name to see news on that
specific topic.

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  * * * * * * * * * * * * * * STN  Columbus  * * * * * * * * * * * * * * *

FILE 'HOME' ENTERED AT 13:07:12 ON 01 JUL 2003

=> file reg
COST IN U.S. DOLLARS                                SINCE FILE     TOTAL
                                                       ENTRY    SESSION
FULL ESTIMATED COST                                     0.21       0.21

FILE 'REGISTRY' ENTERED AT 13:07:21 ON 01 JUL 2003
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Property values tagged with IC are from the ZIC/VINITI data file
provided by InfoChem.

STRUCTURE FILE UPDATES:   30 JUN 2003  HIGHEST RN 540462-79-1
DICTIONARY FILE UPDATES:  30 JUN 2003  HIGHEST RN 540462-79-1

TSCA INFORMATION NOW CURRENT THROUGH JANUARY 6, 2003

  Please note that search-term pricing does apply when
  conducting SmartSELECT searches.

Crossover limits have been increased.  See HELP CROSSOVER for details.

Experimental and calculated property data are now available.  See HELP
PROPERTIES for more information.  See STNote 27, Searching Properties
in the CAS Registry File, for complete details:
http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf

=>
Uploading 10023099.str

L1      STRUCTURE UPLOADED

=> d l1
L1 HAS NO ANSWERS
L1              STR
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10/ 023,099

Welcome to STN International! Enter x:x

LOGINID:ssspta1202txn

PASSWORD:
TERMINAL (ENTER 1, 2, 3, OR ?):2

* * * * * * * * * * Welcome to STN International * * * * * * * * * *

NEWS 1		Web Page URLs for STN Seminar Schedule - N. America
NEWS 2		"Ask CAS" for self-help around the clock
NEWS 3	Jun 03	New e-mail delivery for search results now available
NEWS 4	Aug 08	PHARMAMarketLetter(PHARMAML) - new on STN
NEWS 5	Aug 19	Aquatic Toxicity Information Retrieval (AQUIRE) now available on STN
NEWS 6	Aug 26	Sequence searching in REGISTRY enhanced
NEWS 7	Sep 03	JAPIO has been reloaded and enhanced
NEWS 8	Sep 16	Experimental properties added to the REGISTRY file
NEWS 9	Sep 16	CA Section Thesaurus available in CAPLUS and CA
NEWS 10	Oct 01	CASREACT Enriched with Reactions from 1907 to 1985
NEWS 11	Oct 24	BEILSTEIN adds new search fields
NEWS 12	Oct 24	Nutraceuticals International (NUTRACEUT) now available on STN
NEWS 13	Nov 18	DKILIT has been renamed APOLLIT
NEWS 14	Nov 25	More calculated properties added to REGISTRY
NEWS 15	Dec 04	CSA files on STN
NEWS 16	Dec 17	PCTFULL now covers WP/PCT Applications from 1978 to date
NEWS 17	Dec 17	TOXCENTER enhanced with additional content
NEWS 18	Dec 17	Adis Clinical Trials Insight now available on STN
NEWS 19	Jan 29	Simultaneous left and right truncation added to COMPENDEX, ENERGY, INSPEC
NEWS 20	Feb 13	CANCERLIT is no longer being updated
NEWS 21	Feb 24	METADEX enhancements
NEWS 22	Feb 24	PCTGEN now available on STN
NEWS 23	Feb 24	TEMA now available on STN
NEWS 24	Feb 26	NTIS now allows simultaneous left and right truncation
NEWS 25	Feb 26	PCTFULL now contains images
NEWS 26	Mar 04	SDI PACKAGE for monthly delivery of multifile SDI results
NEWS 27	Mar 20	EVENTLINE will be removed from STN
NEWS 28	Mar 24	PATDPAFULL now available on STN
NEWS 29	Mar 24	Additional information for trade-named substances without structures available in REGISTRY
NEWS 30	Apr 11	Display formats in DGENE enhanced
NEWS 31	Apr 14	MEDLINE Reload
NEWS 32	Apr 17	Polymer searching in REGISTRY enhanced
NEWS 33	Jun 13	Indexing from 1947 to 1956 added to records in CA/CAPLUS
NEWS 34	Apr 21	New current-awareness alert (SDI) frequency in WPIDS/WPINDEX/WPIX
NEWS 35	Apr 28	RDISCLOSURE now available on STN
NEWS 36	May 05	Pharmacokinetic information and systematic chemical names added to PHAR
NEWS 37	May 15	MEDLINE file segment of TOXCENTER reloaded
NEWS 38	May 15	Supporter information for ENCOMPPAT and ENCOMPLIT updated
NEWS 39	May 16	CHEMREACT will be removed from STN
NEWS 40	May 19	Simultaneous left and right truncation added to WSCA
NEWS 41	May 19	RAPRA enhanced with new search field, simultaneous left and right truncation
NEWS 42	Jun 06	Simultaneous left and right truncation added to CBNB
NEWS 43	Jun 06	PASCAL enhanced with additional data
NEWS 44	Jun 20	2003 edition of the FSTA Thesaurus is now available

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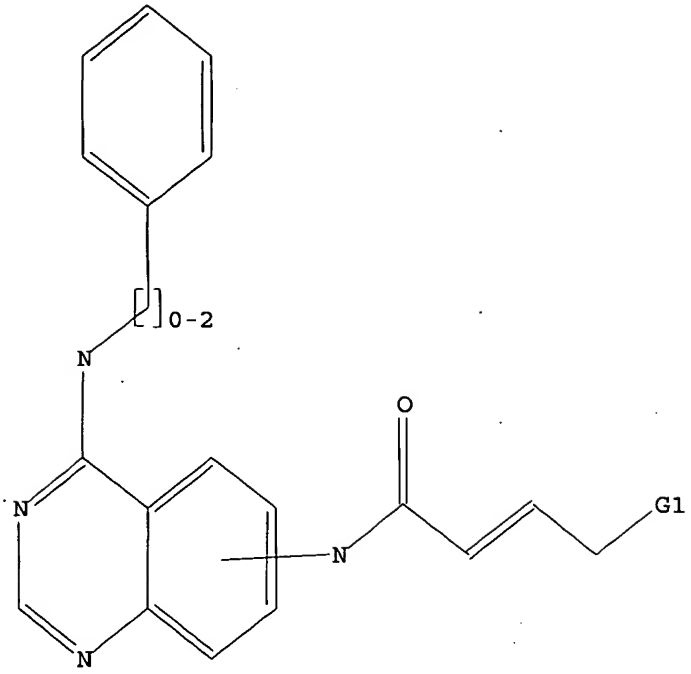

G1 N,Hy

Structure attributes must be viewed using STN Express query preparation.

=> s l1 ful
FULL SEARCH INITIATED 13:07:44 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 792 TO ITERATE

100.0% PROCESSED 792 ITERATIONS 306 ANSWERS
SEARCH TIME: 00.00.01

L2 306 SEA SSS FUL L1

=> file caplus
COST IN U.S. DOLLARS SINCE FILE ENTRY TOTAL SESSION
FULL ESTIMATED COST 148.15 148.36

FILE 'CAPLUS' ENTERED AT 13:07:58 ON 01 JUL 2003
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FILE COVERS 1907 - 1 Jul 2003 VOL 139 ISS 1

10/ 023,099

FILE LAST UPDATED: 30 Jun 2003 (20030630/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> s l2
L3 13 L2

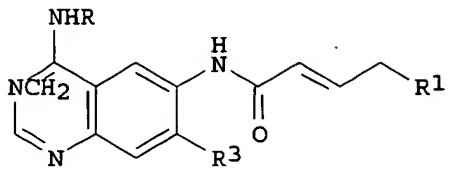
=> d l3 1- ibib abs hitstr
YOU HAVE REQUESTED DATA FROM 13 ANSWERS - CONTINUE? Y/(N):y

L3 ANSWER 1 OF 13 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2002:487536 CAPLUS
DOCUMENT NUMBER: 137:63250
TITLE: Quinazoline derivatives as inhibitors of human EFG tyrosine kinase
INVENTOR(S): Himmelsbach, Frank; Langkopf, Elke; Blech, Stefan; Jung, Birgit; Baum, Elke; Solca, Flavio
PATENT ASSIGNEE(S): Boehringer Ingelheim Pharma Kg, Germany
SOURCE: PCT Int. Appl., 64 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002050043	A1	20020627	WO 2001-EP14569	20011212
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
DE 10063435	A1	20020704	DE 2000-10063435	20001220
AU 2002019174	A5	20020701	AU 2002-19174	20011212
US 2002173509	A1	20021121	US 2001-23099	20011217

PRIORITY APPLN. INFO.: DE 2000-10063435 A 20001220
US 2000-259201P P 20001228
WO 2001-EP14569 W 20011212
OTHER SOURCE(S): MARPAT 137:63250
GI

Pregrant Version



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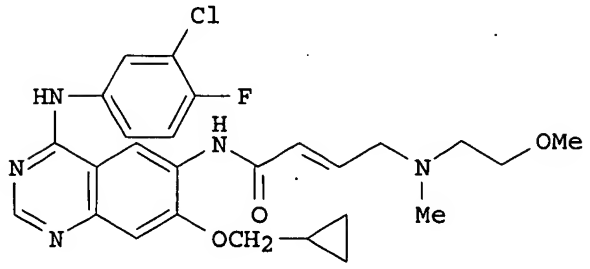


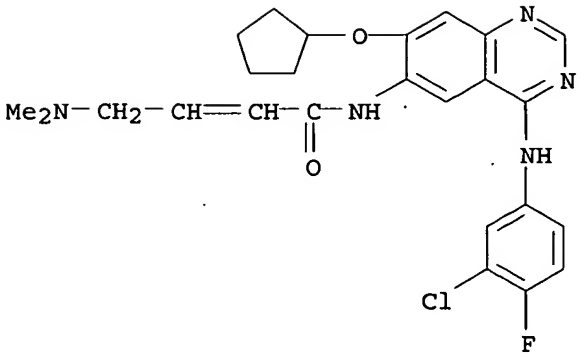
II

AB Quinazoline derivs. I [R = PhCH2, PhCHMe, 3,4-Cl(F)C6H3; R1 = NMeR2, NEt2, NEtCH2CH2OMe, N(CH2CH2OMe)2, morpholino; R2 = Me, Et, CHMe2, cyclopropyl, CH2CH2OMe, 3-tetrahydrofuryl, 2-tetrahydrofurylmethyl, 3-tetrahydrofurylmethyl, 4-tetrahydropyranyl, 4-tetrahydropyranylmethyl; R3 = cyclopropylmethoxy, cyclobutyloxy, cyclopentyloxy, 3-tetrahydrofuranyloxy, 2-tetrahydrofuranylmethoxy, 3-tetrahydrofuranylmethoxy, 4-tetrahydropyranyloxy, 4-tetrahydropyranylmethoxy] were prepd. for use as inhibitors of signal transduction caused by human EFG receptor tyrosine kinase. They are useful in the treatment of tumoral diseases, diseases of the lung and the respiratory tract, the gastrointestinal tract, and the gallbladder and bile ducts. Thus, the quinazoline II was prepd. by converting bromocrotonic acid to its chloride, and reaction with 4-[(3-chloro-4-fluorophenyl)amino]-6-amino-7-cyclopropylmethoxyquinazoline, followed by MeNHCH2CH2OMe. II had an IC50 against human EFG receptor kinase of 0.7 nM.

IT **439081-10-4P 439081-11-5P 439081-13-7P**
439081-18-2P 439081-30-8P 439081-40-0P
439081-41-1P 439081-42-2P 439081-48-8P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of quinazoline derivs. as inhibitors of human EFG tyrosine kinase)

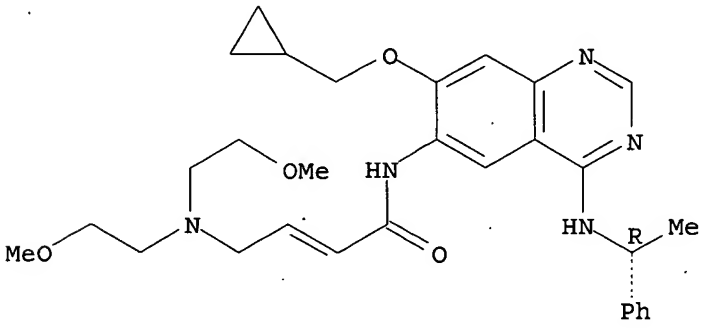
RN 439081-10-4 CAPLUS

CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopentyloxy)-6-quinazolinyl]-4-(dimethylamino)- (9CI) (CA INDEX NAME)



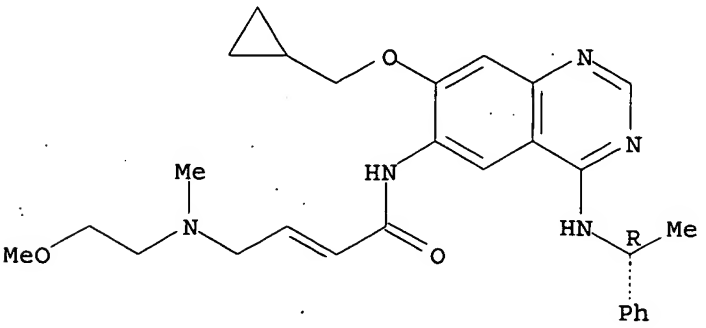
RN 439081-11-5 CAPLUS
CN 2-Butenamide, 4-[bis(2-methoxyethyl)amino]-N-[7-(cyclopropylmethoxy)-4-[[(1R)-1-phenylethyl]amino]-6-quinazolinyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



RN 439081-13-7 CAPLUS
CN 2-Butenamide, N-[7-(cyclopropylmethoxy)-4-[[(1R)-1-phenylethyl]amino]-6-quinazolinyl]-4-[(2-methoxyethyl)methylamino]- (9CI) (CA INDEX NAME)

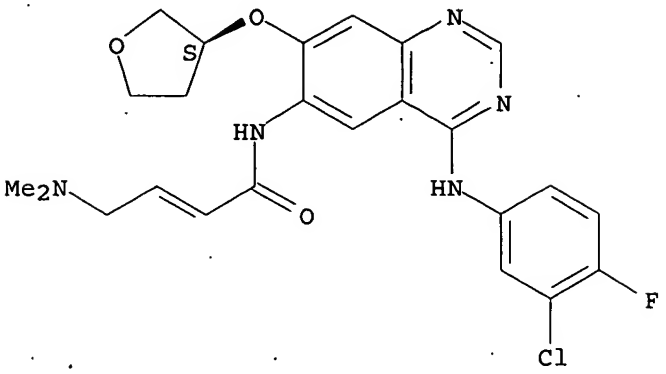
Absolute stereochemistry.
Double bond geometry unknown.



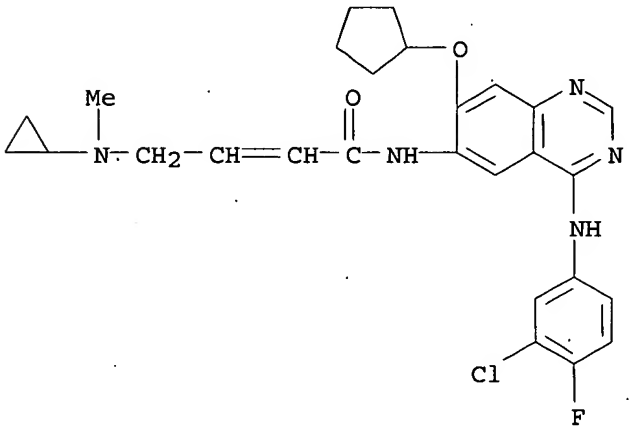
RN 439081-18-2 CAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-[[(3S)-tetrahydro-3-furanyl]oxy]-6-quinazolinyl]-4-(dimethylamino)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry unknown.

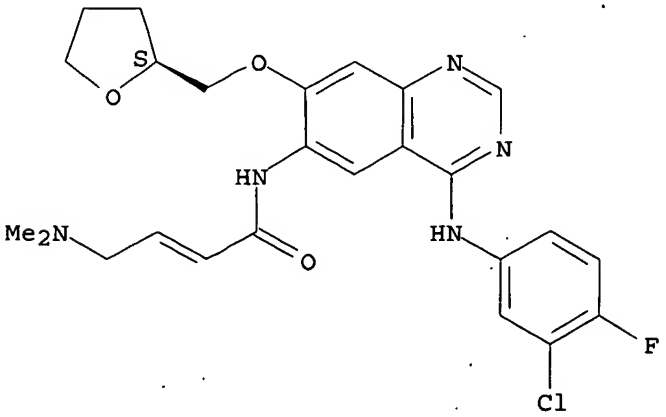


RN 439081-30-8 CAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopentyloxy)-6-quinazolinyl]-4-(cyclopropylmethylamino)- (9CI) (CA INDEX NAME)



RN 439081-40-0 CAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-[[(2S)-tetrahydro-2-furanyl]methoxy]-6-quinazolinyl]-4-(dimethylamino)- (9CI) (CA INDEX NAME)

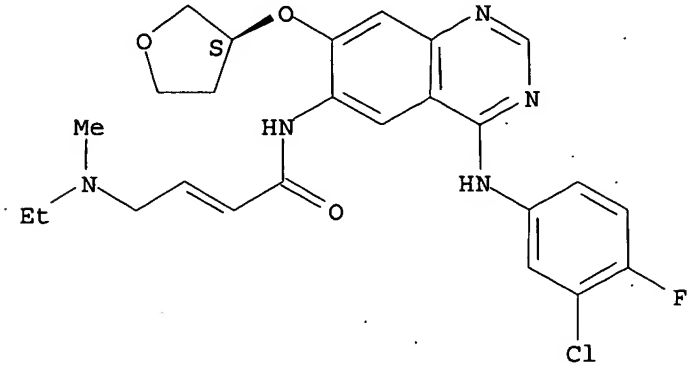
Absolute stereochemistry.
Double bond geometry unknown.



10/ 023,099

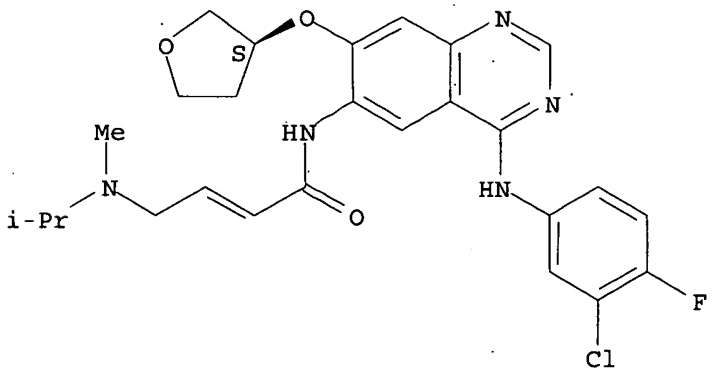
RN 439081-41-1 CAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-[[(3S)-tetrahydro-3-furanyl]oxy]-6-quinazolinyl]-4-(ethylmethylamino)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.

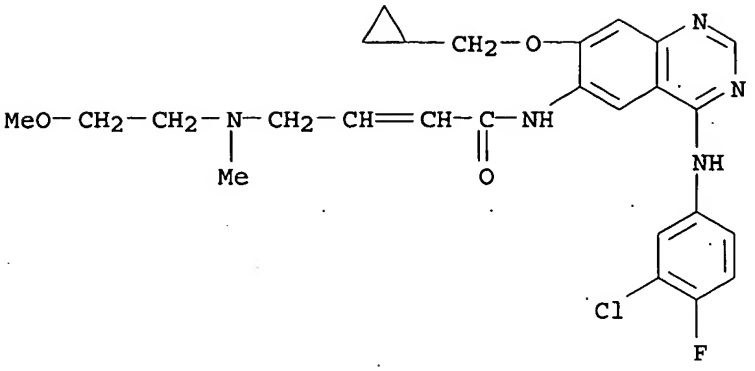


RN 439081-42-2 CAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-[[(3S)-tetrahydro-3-furanyl]oxy]-6-quinazolinyl]-4-[methyl(1-methylethyl)amino]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



RN 439081-48-8 CAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-[(2-methoxyethyl)methylamino]- (9CI) (CA INDEX NAME)



IT **439081-09-1P 439081-12-6P 439081-14-8P**
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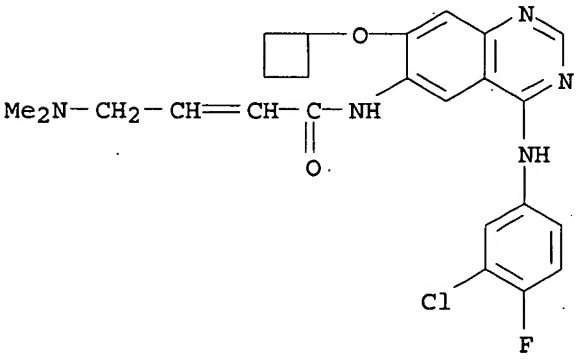
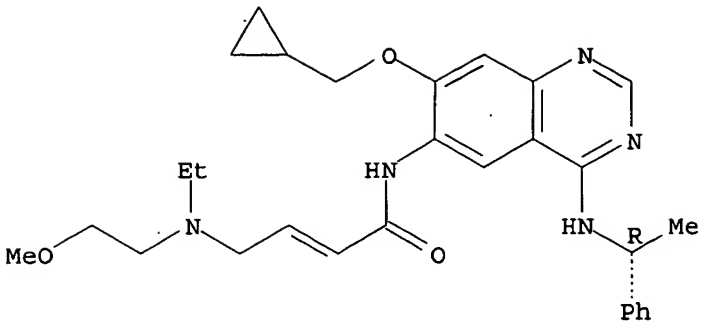
439081-19-3P 439081-20-6P 439081-21-7P
439081-22-8P 439081-23-9P 439081-24-0P
439081-25-1P 439081-26-2P 439081-27-3P
439081-28-4P 439081-29-5P 439081-31-9P
439081-32-0P 439081-33-1P 439081-34-2P
439081-35-3P 439081-36-4P 439081-37-5P
439081-38-6P 439081-39-7P 439081-43-3P
439081-44-4P 439081-45-5P 439081-46-6P
439081-47-7P
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of quinazoline derivs. as inhibitors of human EFG tyrosine kinase)

RN 439081-09-1 CAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclobutyloxy)-6-quinazolinyl]-4-(dimethylamino)- (9CI) (CA INDEX NAME)



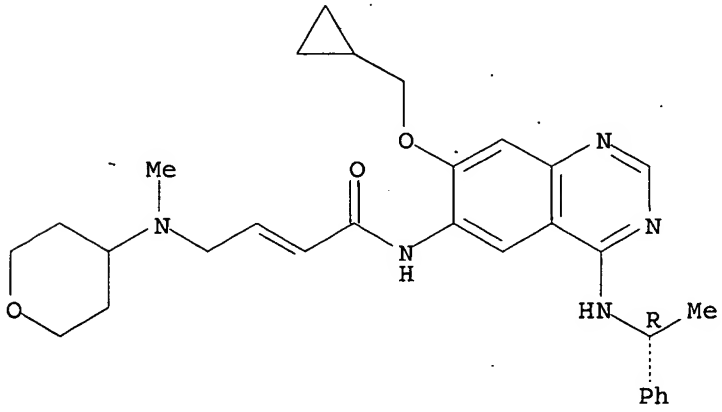
RN 439081-12-6 CAPLUS
CN 2-Butenamide, N-[7-(cyclopropylmethoxy)-4-[[(1R)-1-phenylethyl]amino]-6-quinazolinyl]-4-[ethyl(2-methoxyethyl)amino]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



RN 439081-14-8 CAPLUS
CN 2-Butenamide, N-[7-(cyclopropylmethoxy)-4-[[(1R)-1-phenylethyl]amino]-6-quinazolinyl]-4-[methyl(tetrahydro-2H-pyran-4-yl)amino]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



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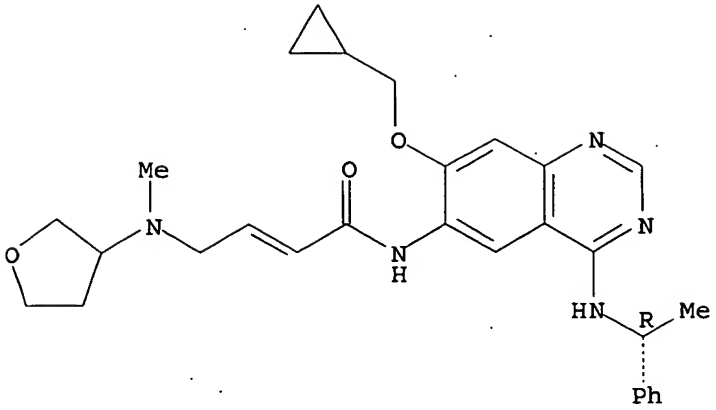
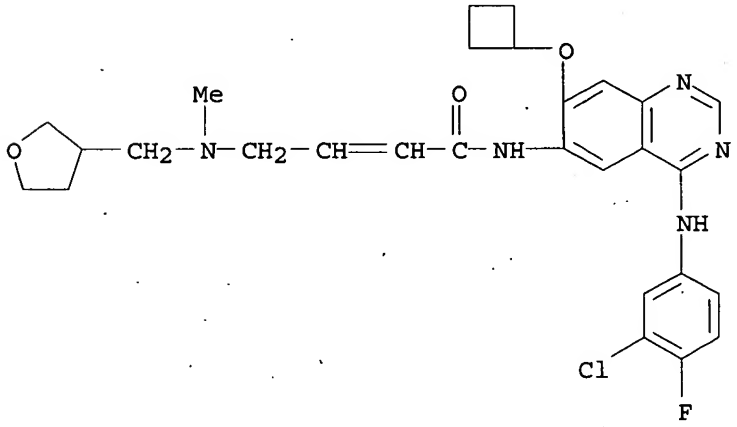
CN 2-Butenamide, N-[7-(cyclopropylmethoxy)-4-[[(1R)-1-phenylethyl]amino]-6-quinazolinyl]-4-[methyl(tetrahydro-3-furanyl)amino]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.

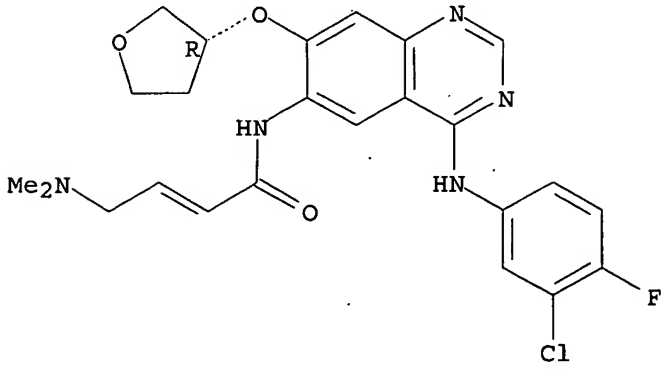


RN 439081-16-0 CAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclobutyloxy)-6-quinazolinyl]-4-[methyl[(tetrahydro-3-furanyl)methyl]amino]- (9CI) (CA INDEX NAME)

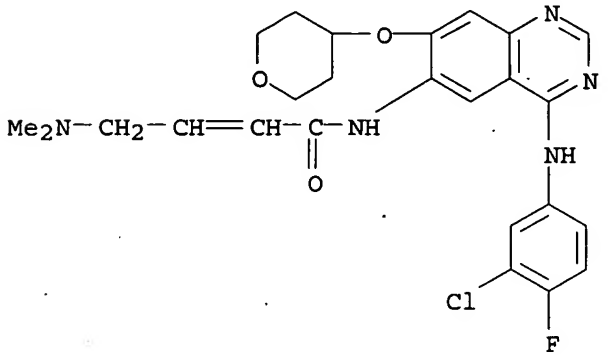


RN 439081-17-1 CAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-[[(3R)-tetrahydro-3-furanyl]oxy]-6-quinazolinyl]-4-(dimethylamino)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



RN 439081-19-3 CAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-[(tetrahydro-2H-pyran-4-yl)oxy]-6-quinazolinyl]-4-(dimethylamino)- (9CI) (CA INDEX NAME)



RN 439081-20-6 CAPLUS
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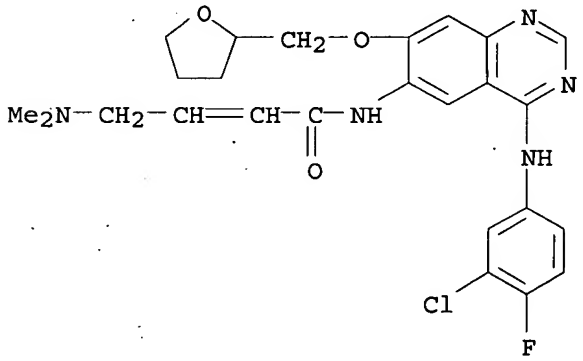

RN 439081-21-7 CAPLUS
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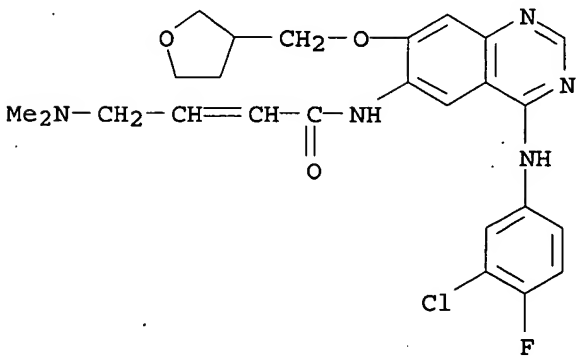
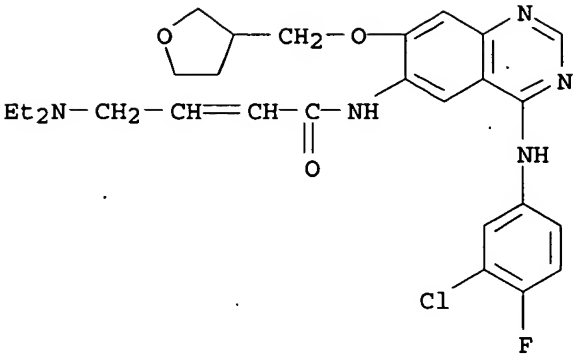
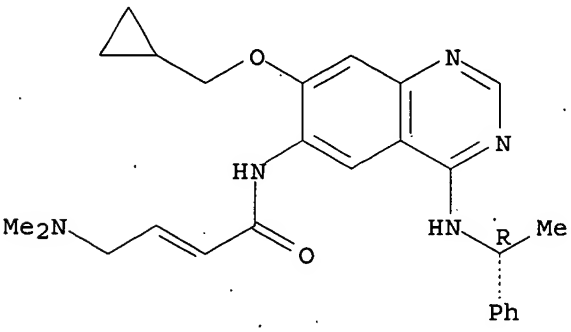


RN 439081-22-8 CAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-[(tetrahydro-3-furanyl)methoxy]-6-quinazolinyl]-4-(diethylamino)- (9CI) (CA INDEX NAME)

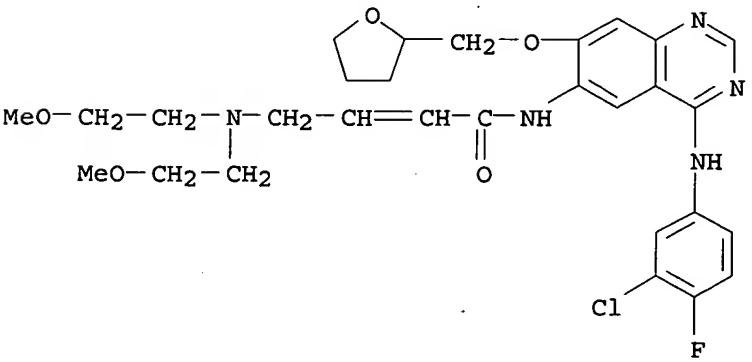


RN 439081-23-9 CAPLUS
CN 2-Butenamide, N-[7-(cyclopropylmethoxy)-4-[[(1R)-1-phenylethyl]amino]-6-quinazolinyl]-4-(dimethylamino)- (9CI) (CA INDEX NAME)

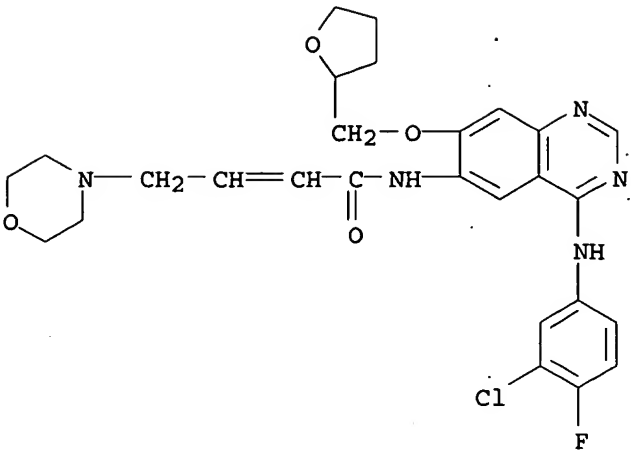
Absolute stereochemistry.
Double bond geometry unknown.



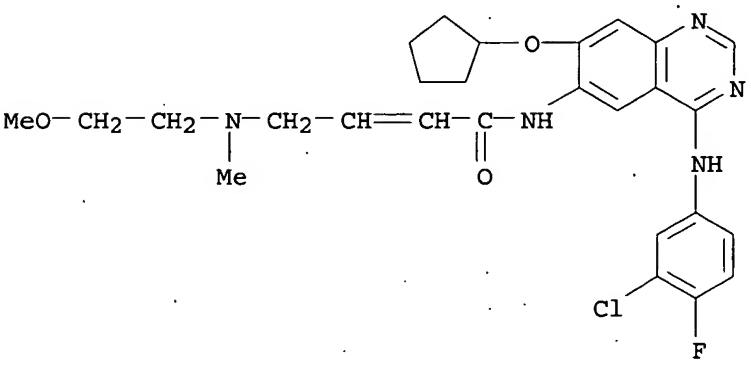
RN 439081-24-0 CAPLUS
CN 2-Butenamide, 4-[bis(2-methoxyethyl)amino]-N-[4-[(3-chloro-4-fluorophenyl)amino]-7-[(tetrahydro-2-furanyl)methoxy]-6-quinazolinyl]- (9CI) (CA INDEX NAME)



RN 439081-25-1 CAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-[(tetrahydro-2-furanyl)methoxy]-6-quinazolinyl]-4-(4-morpholinyl)- (9CI) (CA INDEX NAME)

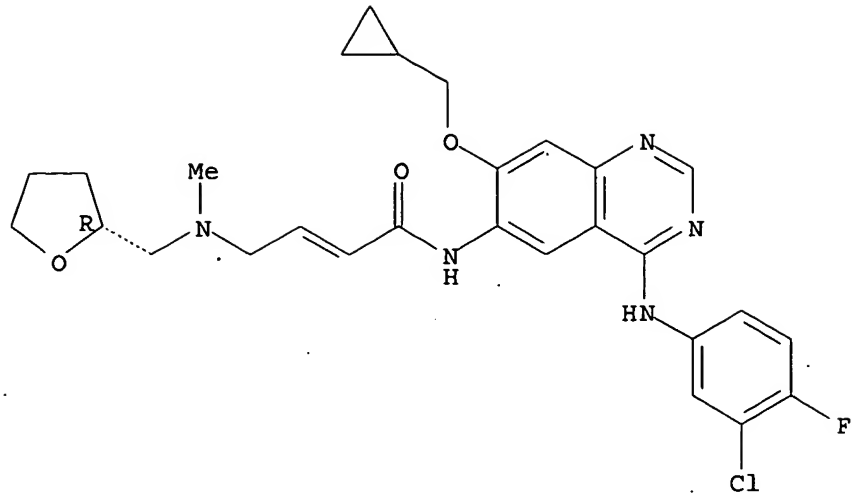


RN 439081-26-2 CAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopentyloxy)-6-quinazolinyl]-4-[(2-methoxyethyl)methylamino]- (9CI) (CA INDEX NAME)



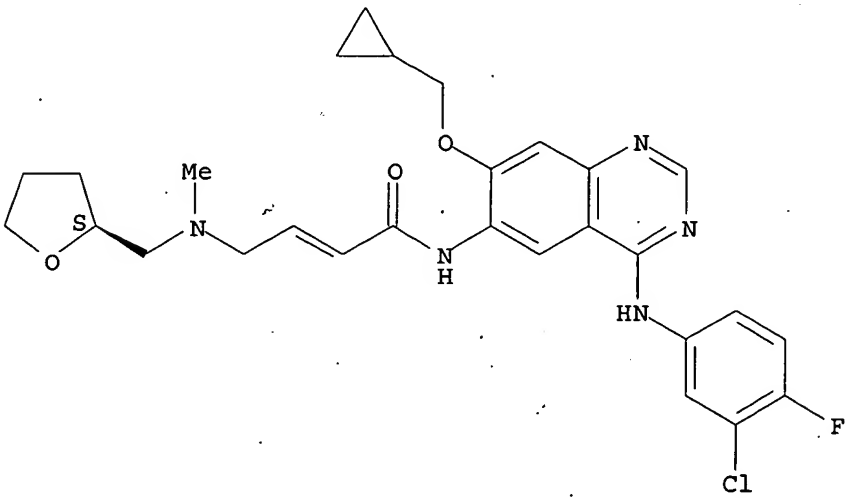
RN 439081-27-3 CAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-[methyl[[(2R)-tetrahydro-2-furanyl]methyl]amino]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



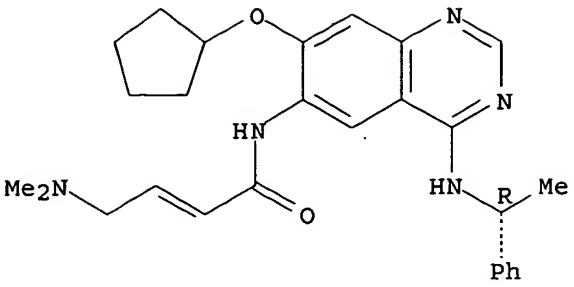
RN 439081-28-4 CAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-[methyl[[(2S)-tetrahydro-2-furanyl]methyl]amino]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.

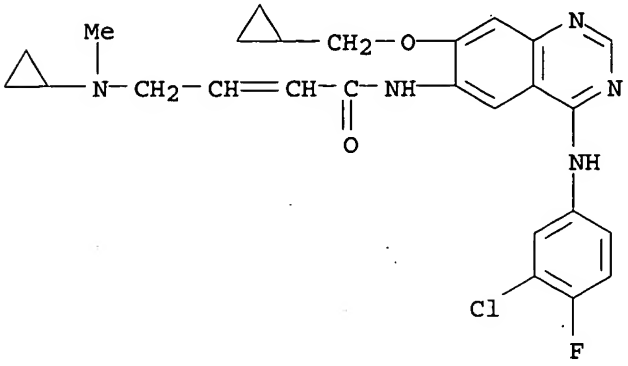


RN 439081-29-5 CAPLUS
CN 2-Butenamide, N-[7-(cyclopentyloxy)-4-[[(1R)-1-phenylethyl]amino]-6-quinazolinyl]-4-(dimethylamino)- (9CI) (CA INDEX NAME)

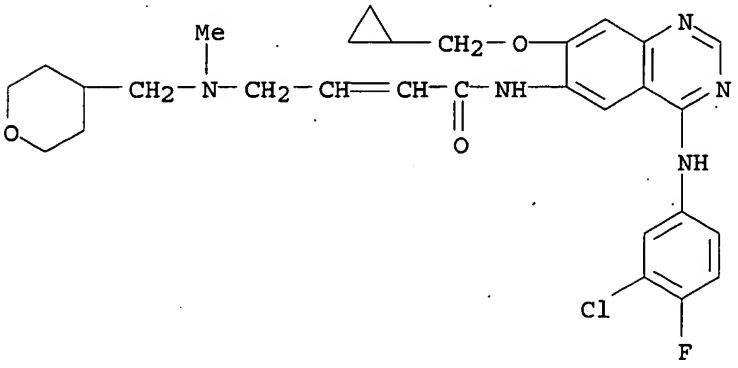
Absolute stereochemistry.
Double bond geometry unknown.



RN 439081-31-9 CAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-(cyclopropylmethylamino)- (9CI) (CA INDEX NAME)

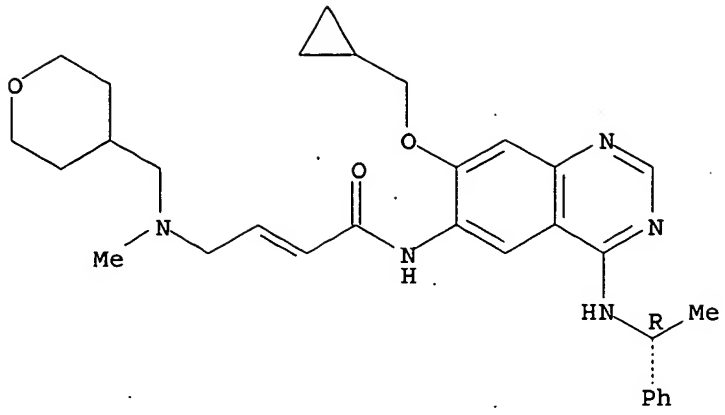


RN 439081-32-0 CAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-[methyl[(tetrahydro-2H-pyran-4-yl)methyl]amino]- (9CI) (CA INDEX NAME)



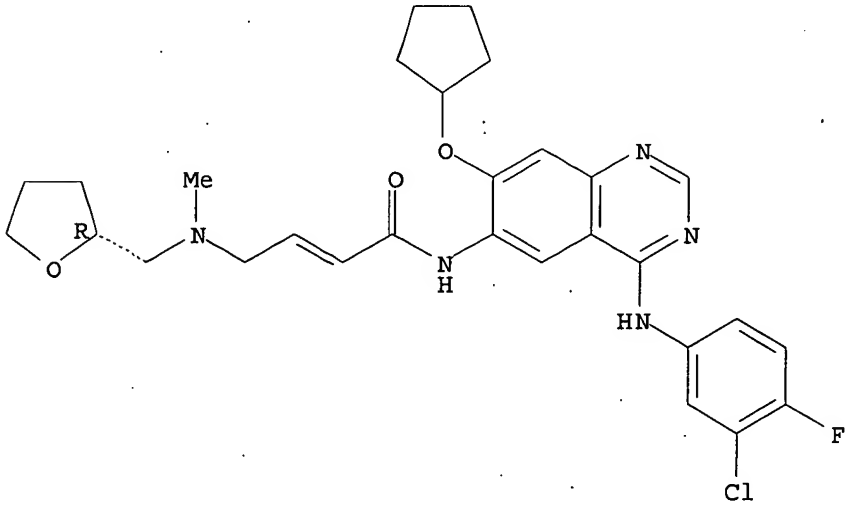
RN 439081-33-1 CAPLUS
CN 2-Butenamide, N-[7-(cyclopropylmethoxy)-4-[[(1R)-1-phenylethyl]amino]-6-quinazolinyl]-4-[methyl[(tetrahydro-2H-pyran-4-yl)methyl]amino]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



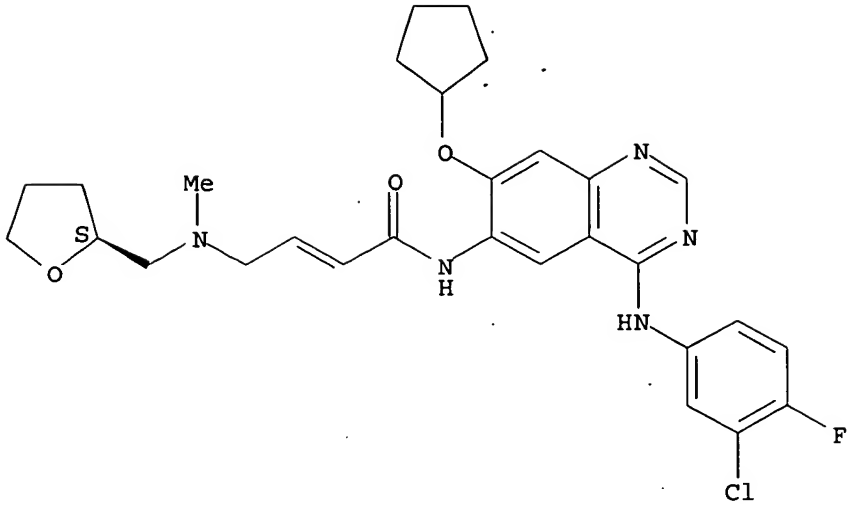
RN 439081-34-2 CAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopentyloxy)-6-quinazolinyl]-4-[methyl[[(2R)-tetrahydro-2-furanyl]methyl]amino]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.

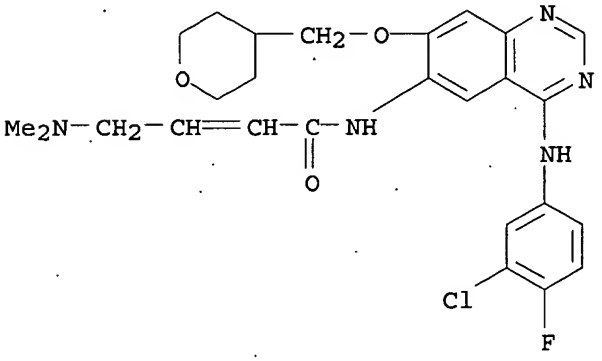


RN 439081-35-3 CAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopentyloxy)-6-quinazolinyl]-4-[methyl[[(2S)-tetrahydro-2-furanyl]methyl]amino]- (9CI) (CA INDEX NAME)

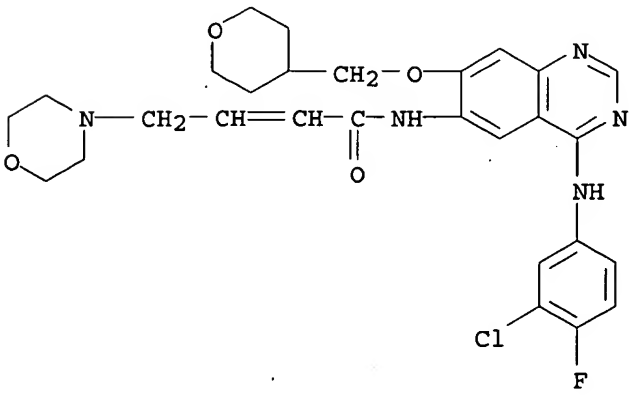
Absolute stereochemistry.
Double bond geometry unknown.



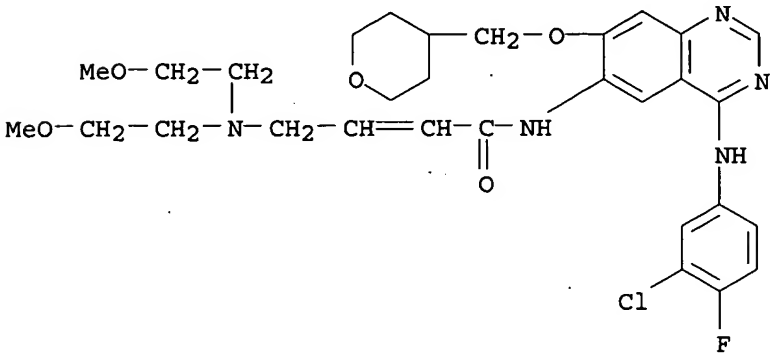
RN 439081-36-4 CAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-[(tetrahydro-2H-pyran-4-yl)methoxy]-6-quinazolinyl]-4-(dimethylamino)- (9CI) (CA INDEX NAME)



RN 439081-37-5 CAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-[(tetrahydro-2H-pyran-4-yl)methoxy]-6-quinazolinyl]-4-(4-morpholinyl)- (9CI) (CA INDEX NAME)

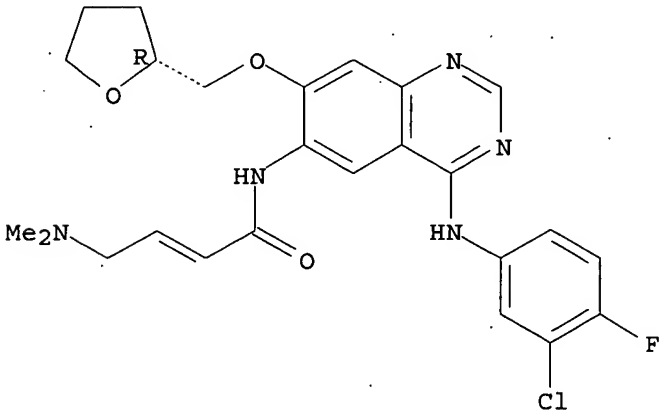


RN 439081-38-6 CAPLUS
CN 2-Butenamide, 4-[bis(2-methoxyethyl)amino]-N-[4-[(3-chloro-4-fluorophenyl)amino]-7-[(tetrahydro-2H-pyran-4-yl)methoxy]-6-quinazolinyl]-(9CI) (CA INDEX NAME)



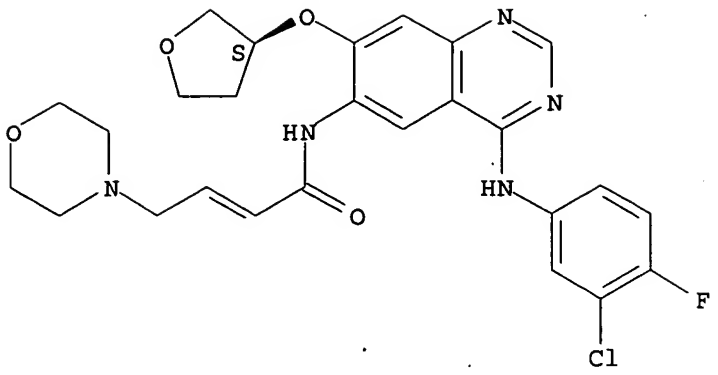
RN 439081-39-7 CAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-[[(2R)-tetrahydro-2-furanyl]methoxy]-6-quinazolinyl]-4-(dimethylamino)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.

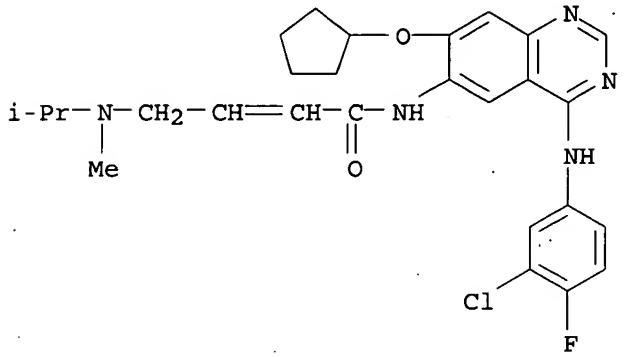


RN 439081-43-3 CAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-[[(3S)-tetrahydro-3-furanyl]oxy]-6-quinazolinyl]-4-(4-morpholinyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.

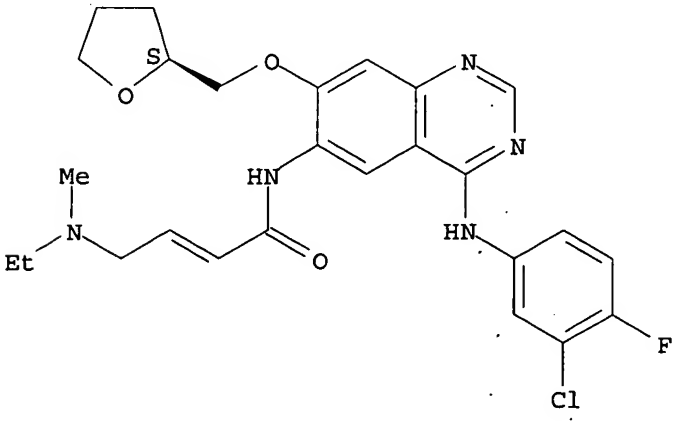


RN 439081-44-4 CAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopentyloxy)-6-quinazolinyl]-4-[methyl(1-methylethyl)amino]- (9CI) (CA INDEX NAME)



RN 439081-45-5 CAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-[[(2S)-tetrahydro-2-furanyl]methoxy]-6-quinazolinyl]-4-(ethylmethylamino)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.

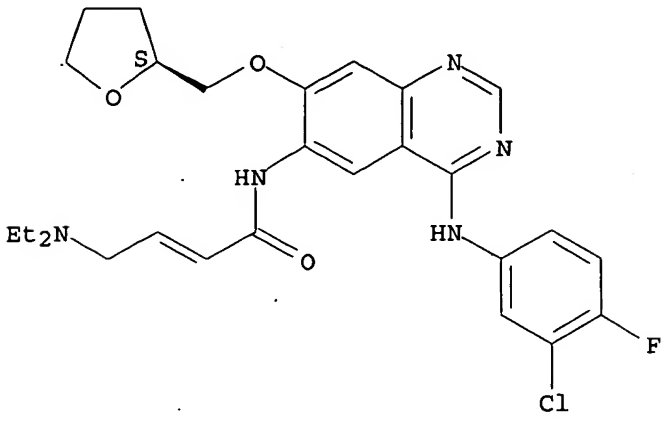


RN 439081-46-6 CAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-[[(2S)-tetrahydro-2-

10/ 023,099

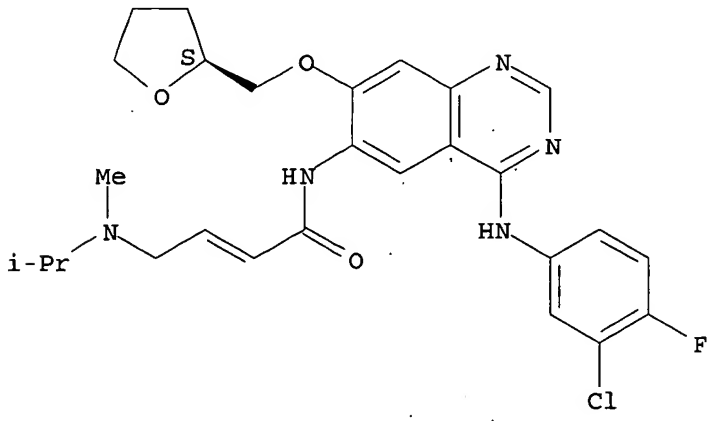
furanyl]methoxy]-6-quinazolinyl]-4-(diethylamino)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



RN 439081-47-7 CAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-[[(2S)-tetrahydro-2-furanyl]methoxy]-6-quinazolinyl]-4-[methyl(1-methylethyl)amino]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 2 OF 13 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2002:171892 CAPLUS
DOCUMENT NUMBER: 136:216762
TITLE: Preparation of 4-amino-6-heterocyclylcarbonylaminoquinazolines as epidermal growth factor receptor signal transduction inhibitors
INVENTOR(S): Himmelsbach, Frank; Langkopf, Elke; Jung, Birgit; Blech, Stefan; Solca, Flavio
PATENT ASSIGNEE(S): Boehringer Ingelheim Pharma Kg, Germany
SOURCE: PCT Int. Appl., 53 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German

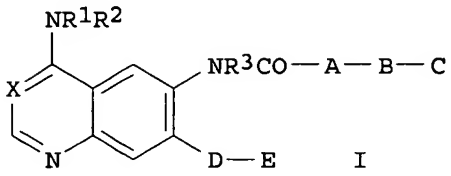
10/ 023,099

FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002018376	A1	20020307	WO 2001-EP9536	20010818
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
DE 10042062	A1	20020307	DE 2000-10042062	20000826
AU 2001095482	A5	20020313	AU 2001-95482	20010818
EP 1315720	A1	20030604	EP 2001-976108	20010818
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
US 2002115675	A1	20020822	US 2001-934631	20010822

PRIORITY APPLN. INFO.: DE 2000-10042062 A 20000826
US 2000-230542P P 20000905
WO 2001-EP9536 W 20010818

OTHER SOURCE(S): MARPAT 136:216762
GI



I

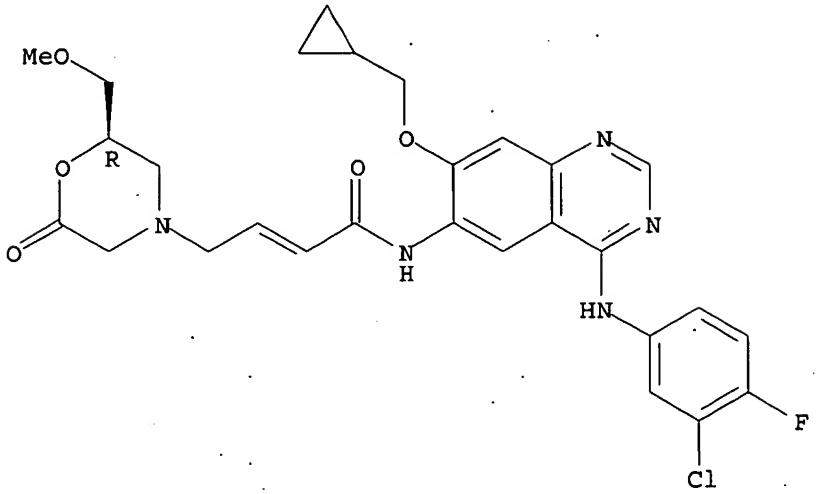
AB Title compds. [I; X = N, (substituted) methynyl; R1 = H, Me; R2 = (substituted) Ph, PhCH2, 1-phenylethyl; R3 = H, Me; A = (substituted) vinyl, ethynyl, 1,3-butadien-1,4-yl; B = (substituted) alkenyl, alkenylcarbonyl, etc.; C = (substituted) 2-oxomorpholin-4-yl, etc; D = oxyalkenyl, O; E = (substituted) amino, alkenylimino, imidazolyl, cycloalkyl; or DE = H, (substituted) alkoxy, etc.], were prepd. Thus, 4-[(3-chloro-4-fluorophenyl)amino]-6-[(4-[N-(ethoxycarbonylmethyl)-N-((R)-2-hydroxy-3-methoxypropyl)amino]-1-oxo-2-buten-1-yl)amino]-7-cyclopropylmethoxyquinazoline (prepn. given) and MeSO2OH in MeCN were stirred for 4 h under reflux to give 69% 4-[(3-chloro-4-fluorophenyl)amino]-6-[(4-[(R)-2-methoxymethyl-6-oxomorpholin-4-yl]-1-oxo-2-buten-1-yl)amino]-7-cyclopropylmethoxyquinazoline. The latter inhibited epidermal growth factor (EGF)-dependent proliferation of F/L-HERc cells with IC50 = 2 nM. The invention relates to the use of the title compds. for treating tumor diseases, and lung and respiratory tract disorders.

IT **402569-98-6P 402569-99-7P 402570-00-7P 402570-01-8P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of (amino)(heterocyclylcarbonylamino)quinazolines as epidermal growth factor receptor signal transduction inhibitors)

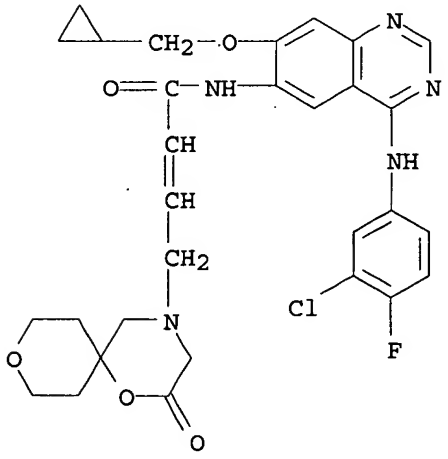
RN 402569-98-6 CAPLUS

CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-[(2R)-2-(methoxymethyl)-6-oxo-4-morpholinyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.

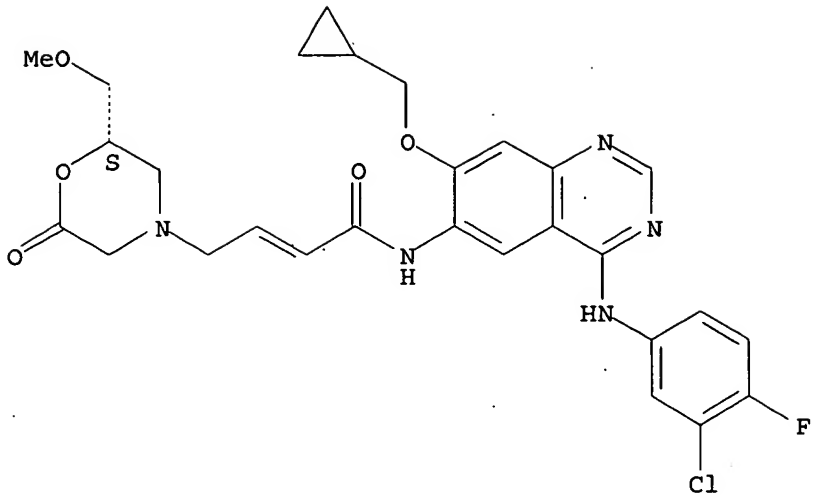


RN 402569-99-7 CAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-(2-oxo-1,9-dioxa-4-azaspiro[5.5]undec-4-yl)- (9CI) (CA INDEX NAME)

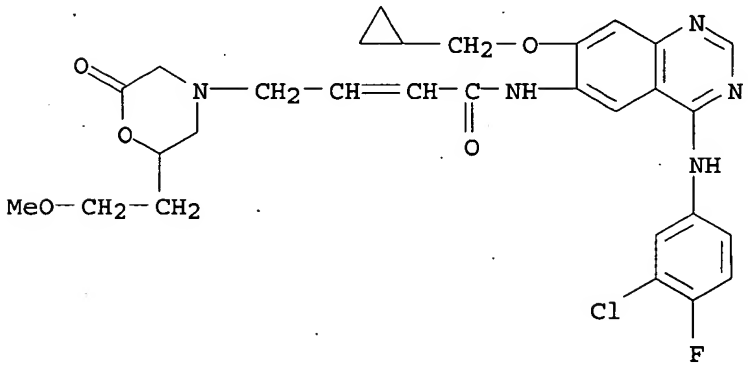


RN 402570-00-7 CAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-[(2S)-2-(methoxymethyl)-6-oxo-4-morpholinyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.

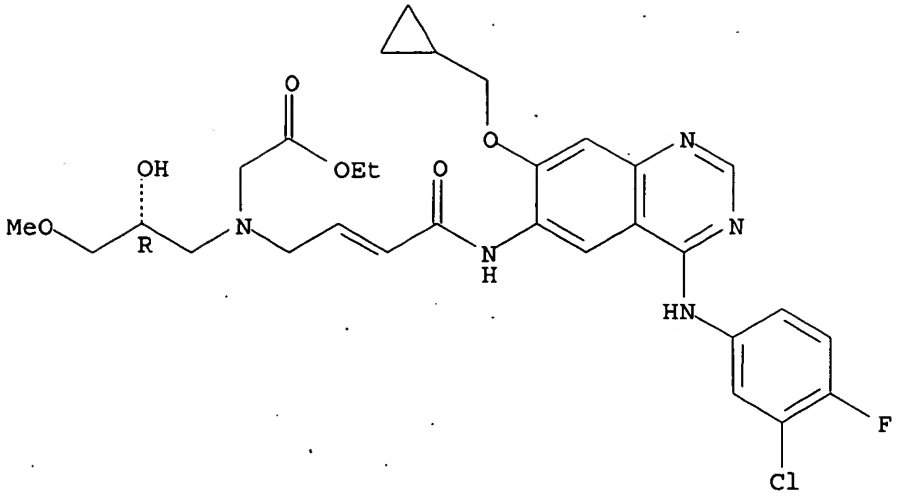


RN 402570-01-8 CAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-[2-(2-methoxyethyl)-6-oxo-4-morpholinyl]- (9CI) (CA INDEX NAME)

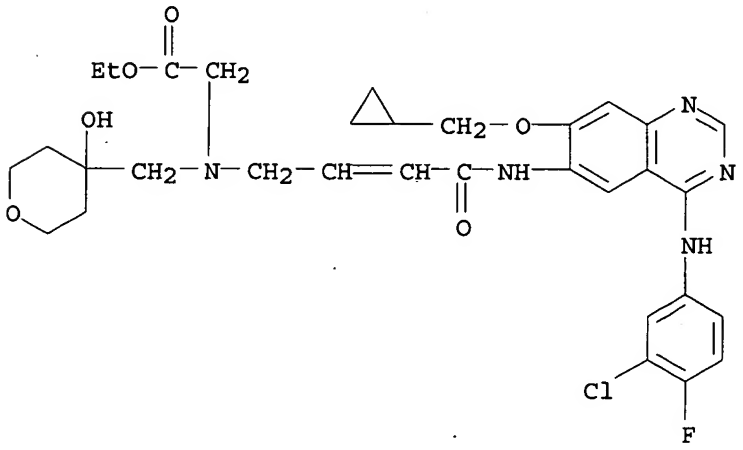


IT **402569-87-3P 402569-89-5P 402569-90-8P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of (amino)(heterocyclylcarbonylamino)quinazolines as epidermal growth factor receptor signal transduction inhibitors)
RN 402569-87-3 CAPLUS
CN Glycine, N-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]amino]-4-oxo-2-butenyl]-N-[(2R)-2-hydroxy-3-methoxypropyl]-, ethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.

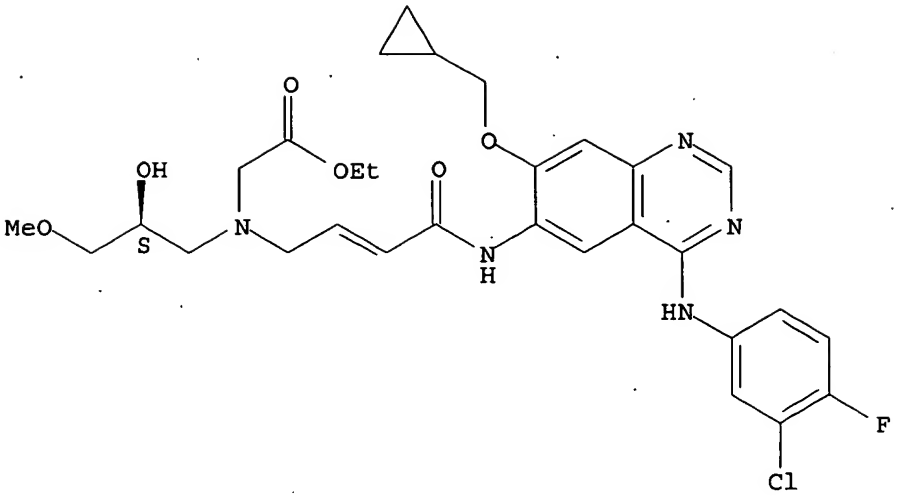


RN 402569-89-5 CAPLUS
CN Glycine, N-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]amino]-4-oxo-2-butenyl]-N-[(tetrahydro-4-hydroxy-2H-pyran-4-yl)methyl]-, ethyl ester (9CI) (CA INDEX NAME)



RN 402569-90-8 CAPLUS
CN Glycine, N-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]amino]-4-oxo-2-butenyl]-N-[(2S)-2-hydroxy-3-methoxypropyl]-, ethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.

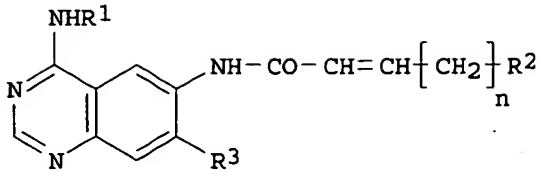


REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 3 OF 13 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2002:171889 CAPLUS
DOCUMENT NUMBER: 136:232315
TITLE: Preparation of 4-amino-6-vinylcarbonylaminoquinazolines as epidermal growth factor receptor signal transduction inhibitors
INVENTOR(S): Himmelsbach, Frank; Langkopf, Elke; Jung, Birgit; Blech, Stefan; Solca, Flavio
PATENT ASSIGNEE(S): Boehringer Ingelheim Pharma Kg, Germany
SOURCE: PCT Int. Appl., 78 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002018373	A1	20020307	WO 2001-EP9537	20010818
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
DE 10042060	A1	20020307	DE 2000-10042060	20000826
US 2002077330	A1	20020620	US 2001-929931	20010815
AU 2001084021	A5	20020313	AU 2001-84021	20010818
EP 1315717	A1	20030604	EP 2001-962953	20010818
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				

PRIORITY APPLN. INFO.: DE 2000-10042060 A 20000826
US 2000-230389P P 20000906
WO 2001-EP9537 W 20010818
OTHER SOURCE(S): MARPAT 136:232315
GI



I

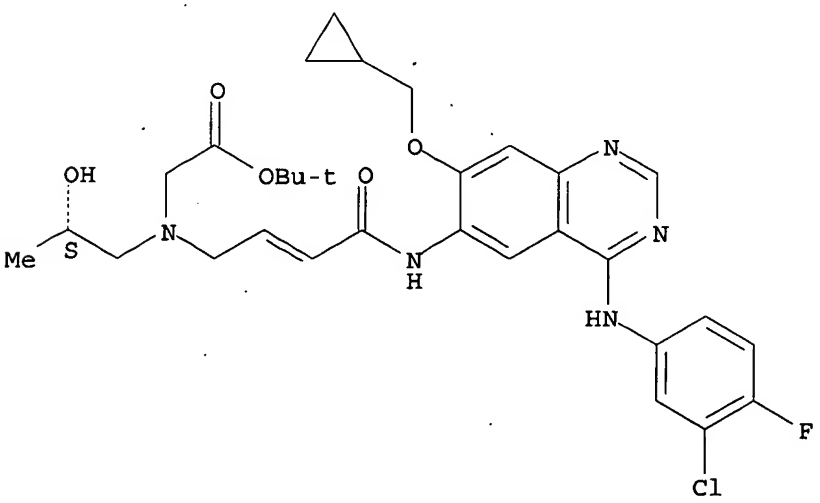
AB Title compds. [I; R1 = PhCH2, 1-phenylethyl, (substituted) Ph; R2 = N-[(1,3-dioxolan-2-yl)methyl]methylamino, (substituted) R4OCOCH2NCH2CH2OH, 2-oxomorpholin-4-yl; R4 = H, alkyl; R3 = H, (alkoxy)alkoxy, cycloalkylalkoxy, tetrahydrofuran-3-yloxy, tetrahydropyran-3-yloxy, tetrahydropyran-4-yloxy, tetrahydrofuranylmethoxy, tetrahydropyranylmethoxy; n = 1-3], were prepd. Thus, a mixt. of 6-amino-4-[(3-chloro-4-fluorophenyl)amino]-7-cyclopropylmethoxyquinazoline (prepn. given) and disopropylethylamine in THF was dropwise treated under ice-cooling with BrCH2CH:CHCO2Cl (prepn. given) in CH2Cl2 followed by stirring for 1 h under ice-cooling and for 2 h at room temp. and addn. of (S)-(2-hydroxypropylamino)acetic acid tert-Bu ester in CH2Cl2 to give after stirring over night at room temp. and stirring for 5 h at 60.degree. 64% 4-[(3-chloro-4-fluorophenyl)amino]-6-[(4-[N-(tert-butyloxycarbonylmethyl)-N-((S)-2-hydroxyprop-1-yl)amino]-1-oxo-2-buten-1-yl)amino]-7-cyclopropylmethoxyquinazoline. Several I inhibited epidermal growth factor (EGF)-dependent proliferation of F/L-HERc cells with IC50 = 0.02-15 nM. The invention relates to the use of the title compds. for treating tumor diseases, and lung and respiratory tract disorders.

IT **402855-15-6P 402855-53-2P**
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(prepn. of (amino)(vinylcarbonylamino)quinazolines as epidermal growth factor receptor signal transduction inhibitors)

RN 402855-15-6 CAPLUS

CN Glycine, N-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]amino]-4-oxo-2-butenyl]-N-[(2S)-2-hydroxypropyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



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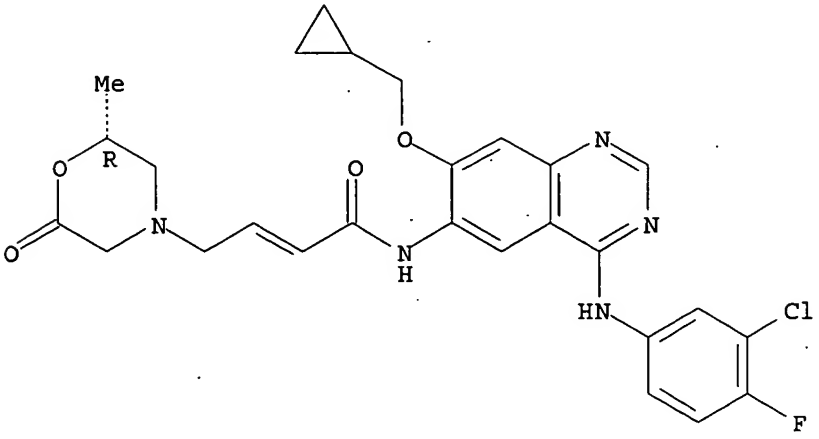
RN 402855-53-2 CAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-[(2R)-2-methyl-6-oxo-4-morpholinyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



IT **402855-16-7P 402855-17-8P 402855-18-9P**
402855-19-0P 402855-20-3P 402855-21-4P
402855-22-5P 402855-23-6P 402855-24-7P
402855-25-8P 402855-26-9P 402855-27-0P
402855-28-1P 402855-29-2P 402855-30-5P
402855-31-6P 402855-32-7P 402855-33-8P
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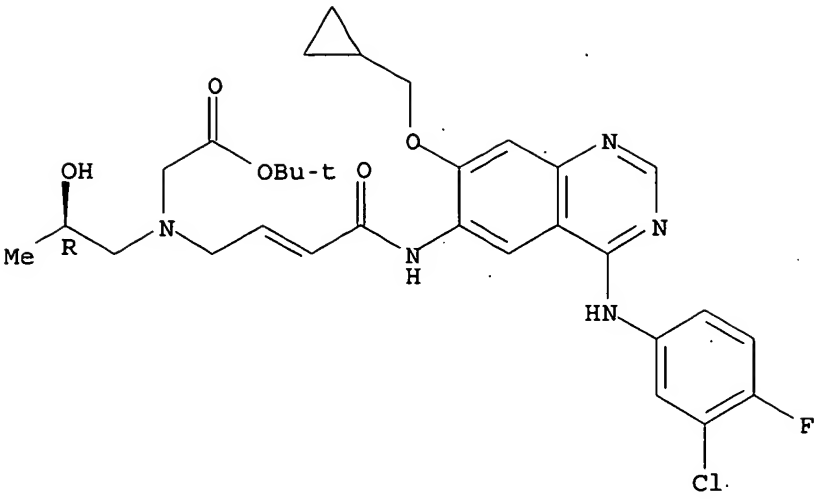
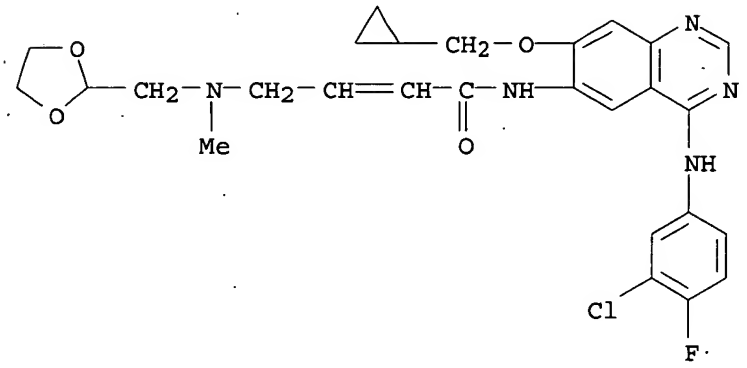
402855-74-7P 402855-75-8P 402855-76-9P
402855-77-0P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of (amino)(vinylcarbonylamino)quinazolines as epidermal growth factor receptor signal transduction inhibitors)

RN 402855-16-7 CAPLUS
CN Glycine, N-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]amino]-4-oxo-2-butenyl]-N-[(2R)-2-hydroxypropyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.

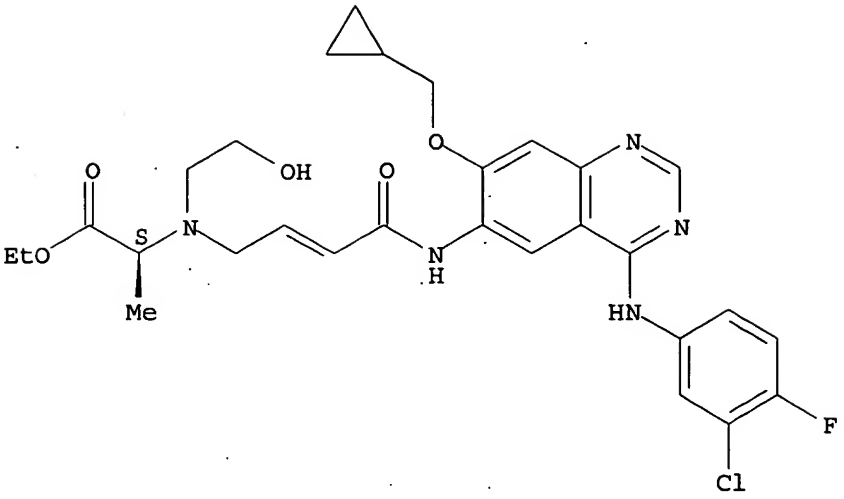


RN 402855-17-8 CAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-[(1,3-dioxolan-2-ylmethyl)methylamino]- (9CI) (CA INDEX NAME)

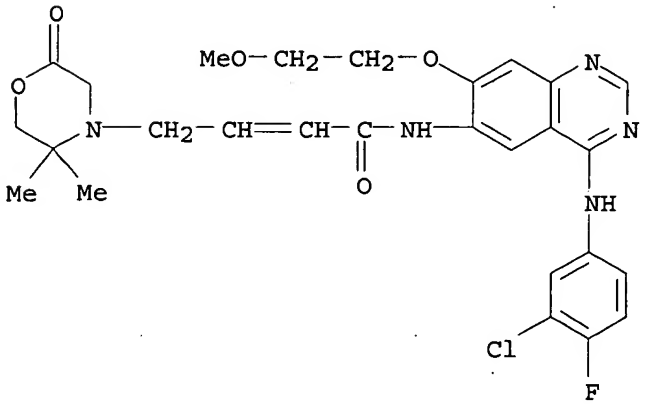


RN 402855-18-9 CAPLUS
CN L-Alanine, N-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]amino]-4-oxo-2-butenyl]-N-(2-hydroxyethyl)-, ethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.

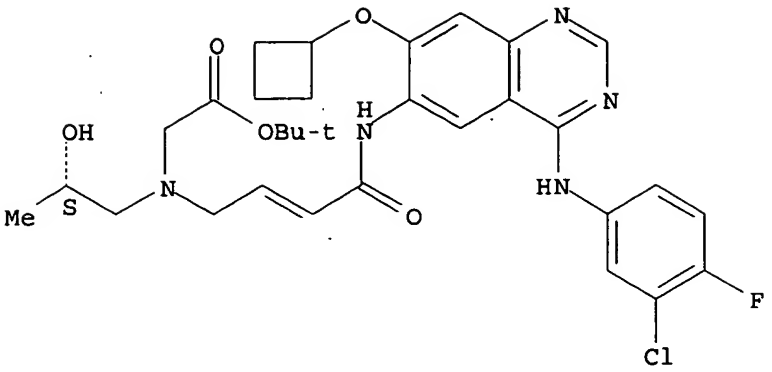


RN 402855-19-0 CAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(2-methoxyethoxy)-6-quinazolinyl]-4-(5,5-dimethyl-2-oxo-4-morpholinyl)- (9CI) (CA INDEX NAME)



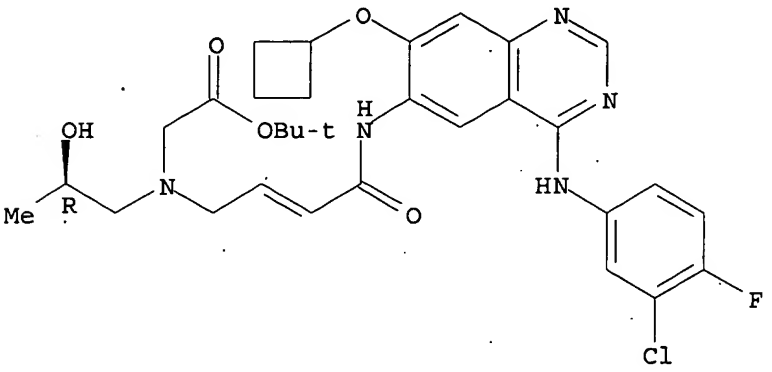
RN 402855-20-3 CAPLUS
CN Glycine, N-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclobutyloxy)-6-quinazolinyl]amino]-4-oxo-2-butenyl]-N-[(2S)-2-hydroxypropyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.

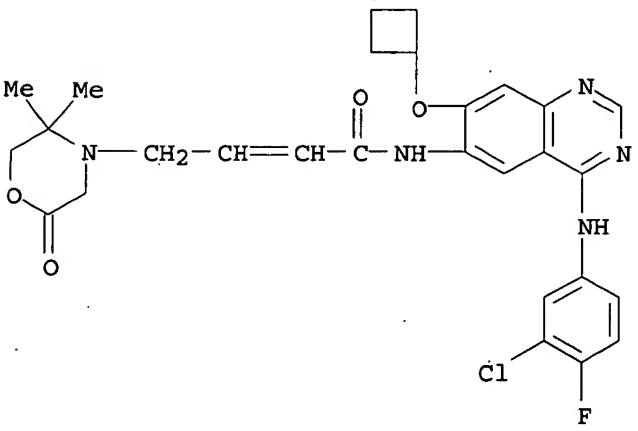


RN 402855-21-4 CAPLUS
CN Glycine, N-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclobutyloxy)-6-quinazolinyl]amino]-4-oxo-2-butenyl]-N-[(2R)-2-hydroxypropyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



RN 402855-22-5 CAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclobutyloxy)-6-quinazolinyl]-4-(5,5-dimethyl-2-oxo-4-morpholinyl)- (9CI) (CA INDEX NAME)



RN 402855-23-6 CAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopentyloxy)-6-

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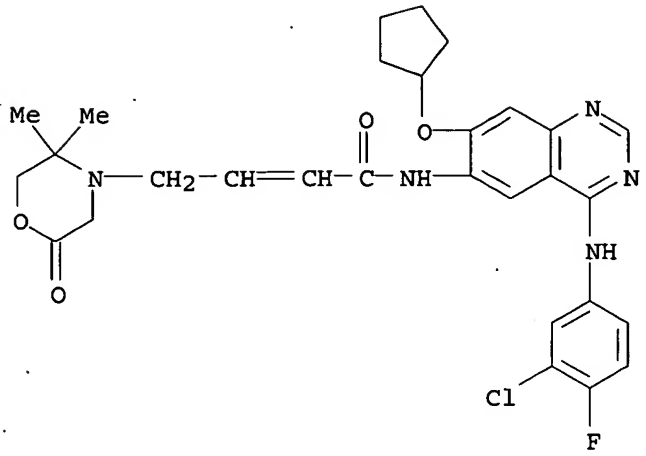
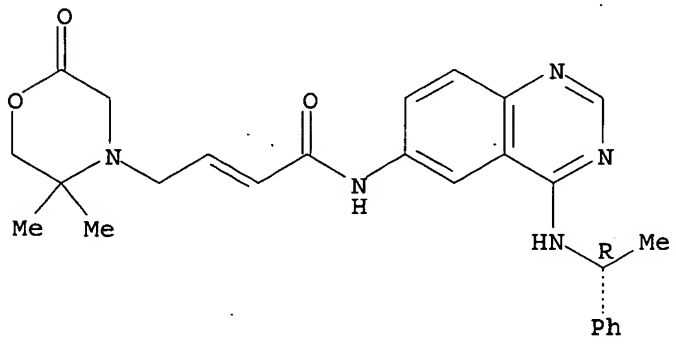
quinazolinyl]-4-(5,5-dimethyl-2-oxo-4-morpholinyl)- (9CI) (CA INDEX NAME)



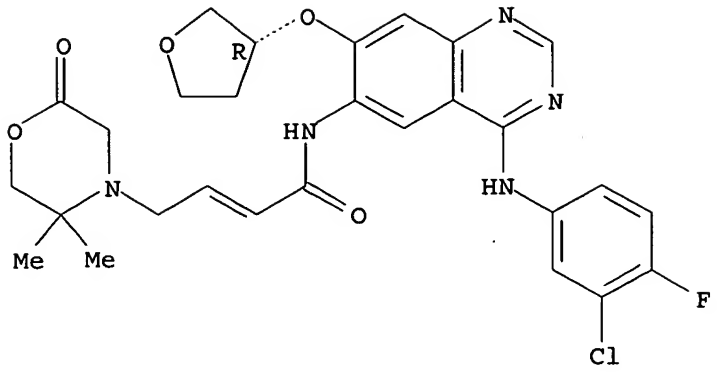
RN 402855-24-7 CAPLUS
CN 2-Butenamide, 4-(5,5-dimethyl-2-oxo-4-morpholinyl)-N-[4-[[(1R)-1-phenylethyl]amino]-6-quinazolinyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



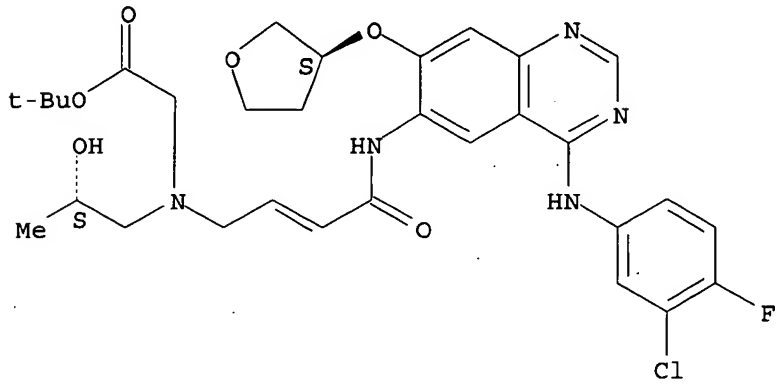
RN 402855-25-8 CAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-[[(3R)-tetrahydro-3-furanyl]oxy]-6-quinazolinyl]-4-(5,5-dimethyl-2-oxo-4-morpholinyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



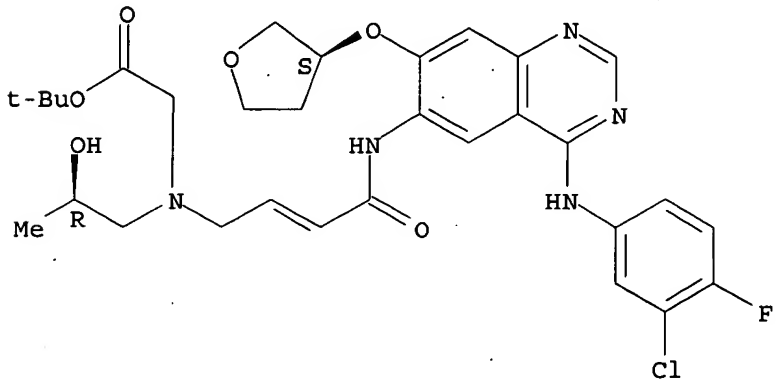
RN 402855-26-9 CAPLUS
CN Glycine, N-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-[[(3S)-tetrahydro-3-furanyl]oxy]-6-quinazolinyl]amino]-4-oxo-2-butenyl]-N-[(2S)-2-hydroxypropyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



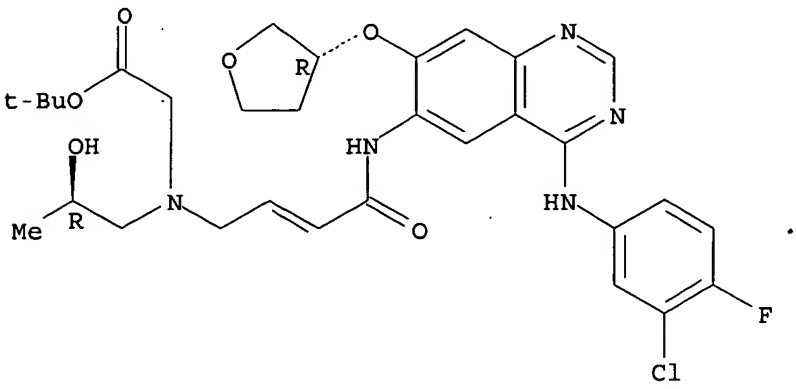
RN 402855-27-0 CAPLUS
CN Glycine, N-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-[[(3S)-tetrahydro-3-furanyl]oxy]-6-quinazolinyl]amino]-4-oxo-2-butenyl]-N-[(2R)-2-hydroxypropyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.

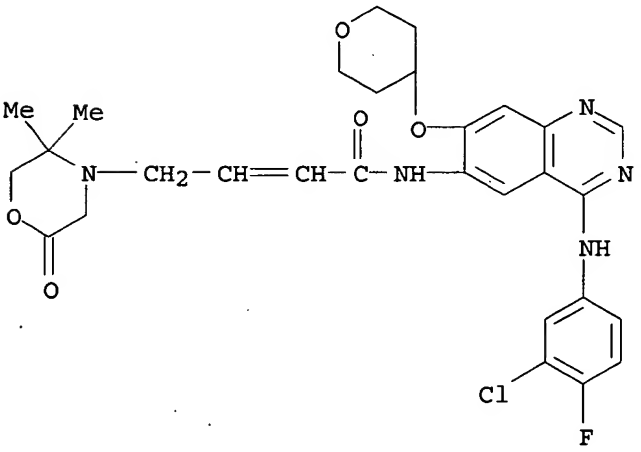


RN 402855-28-1 CAPLUS
CN Glycine, N-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-[[(3R)-tetrahydro-3-furanyl]oxy]-6-quinazolinyl]amino]-4-oxo-2-butenyl]-N-[(2R)-2-hydroxypropyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.

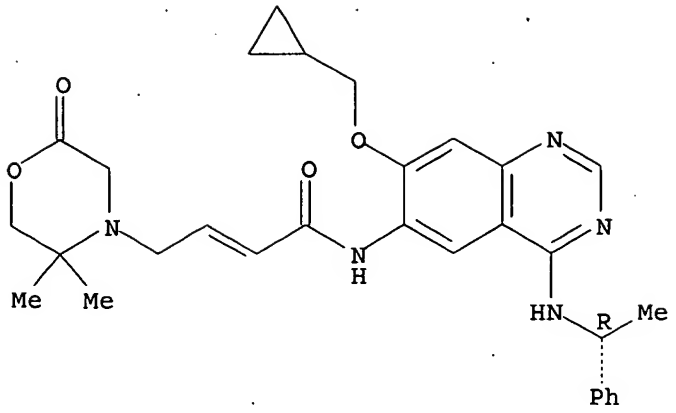


RN 402855-29-2 CAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-[(tetrahydro-2H-pyran-4-yl)oxy]-6-quinazolinyl]-4-(5,5-dimethyl-2-oxo-4-morpholinyl)- (9CI) (CA INDEX NAME)

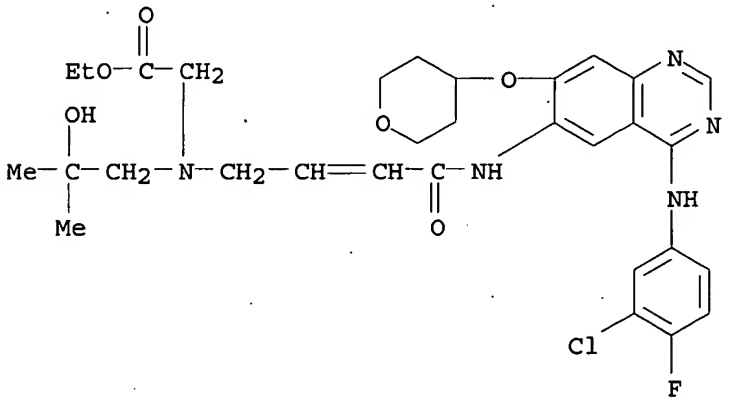


RN 402855-30-5 CAPLUS
CN 2-Butenamide, N-[7-(cyclopropylmethoxy)-4-[[(1R)-1-phenylethyl]amino]-6-quinazolinyl]-4-(5,5-dimethyl-2-oxo-4-morpholinyl)- (9CI) (CA INDEX NAME)

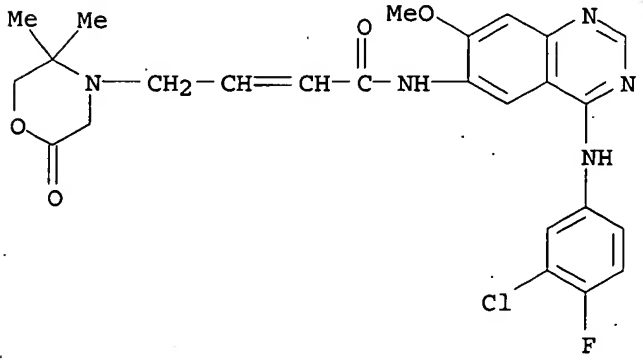
Absolute stereochemistry.
Double bond geometry unknown.



RN 402855-31-6 CAPLUS
CN Glycine, N-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-[(tetrahydro-2H-pyran-4-yl)oxy]-6-quinazolinyl]amino]-4-oxo-2-butenyl]-N-(2-hydroxy-2-methylpropyl)-, ethyl ester (9CI) (CA INDEX NAME)



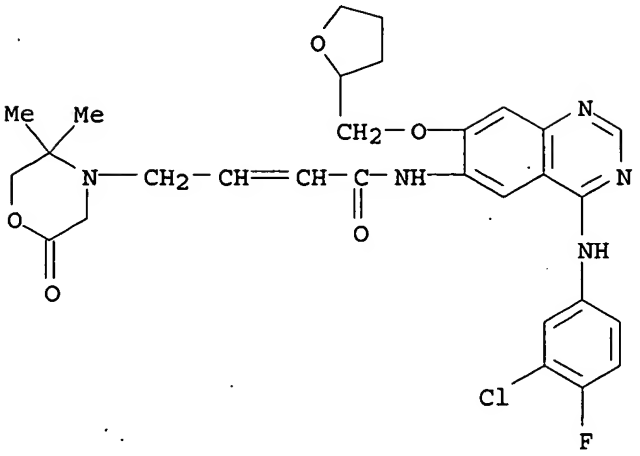
RN 402855-32-7 CAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-methoxy-6-quinazolinyl]-4-(5,5-dimethyl-2-oxo-4-morpholinyl)- (9CI) (CA INDEX NAME)



RN 402855-33-8 CAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-[(tetrahydro-2-furanyl)methoxy]-6-quinazolinyl]-4-(5,5-dimethyl-2-oxo-4-morpholinyl)-

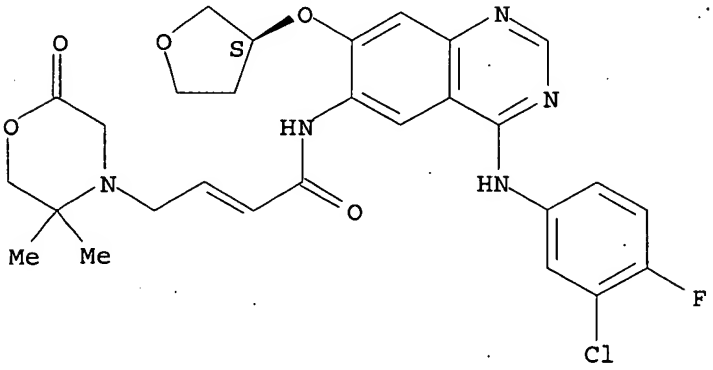
10/ 023,099

(9CI) (CA INDEX NAME)

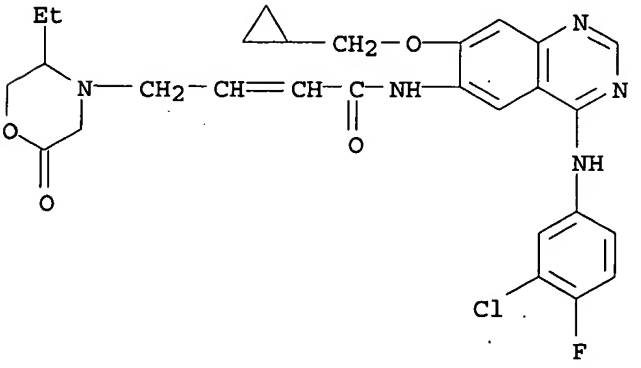


RN 402855-34-9 CAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-[[(3S)-tetrahydro-3-furanyl]oxy]-6-quinazolinyl]-4-(5,5-dimethyl-2-oxo-4-morpholinyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.

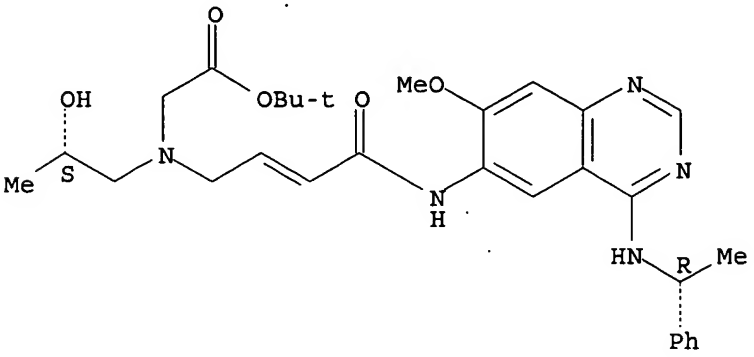


RN 402855-35-0 CAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-(5-ethyl-2-oxo-4-morpholinyl)- (9CI) (CA INDEX NAME)



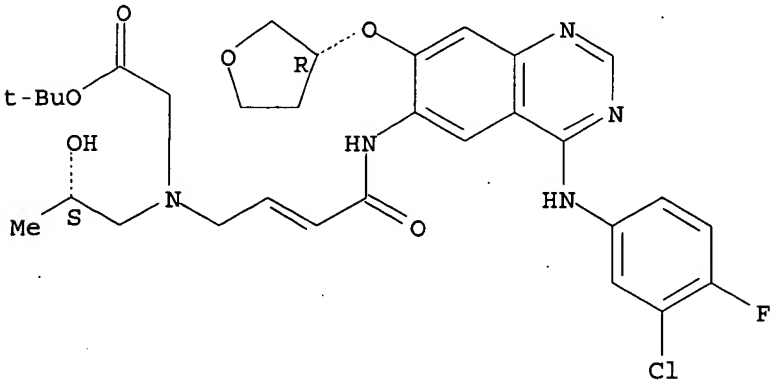
RN 402855-36-1 CAPLUS
CN Glycine, N-[(2S)-2-hydroxypropyl]-N-[4-[[7-methoxy-4-[[(1R)-1-phenylethyl]amino]-6-quinazolinyl]amino]-4-oxo-2-butenyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.

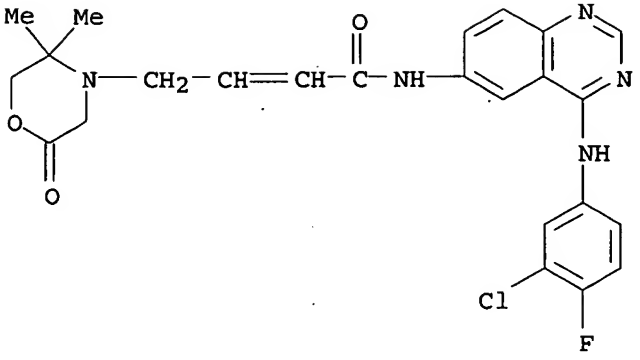


RN 402855-37-2 CAPLUS
CN Glycine, N-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-[[(3R)-tetrahydro-3-furanyl]oxy]-6-quinazolinyl]amino]-4-oxo-2-butenyl]-N-[(2S)-2-hydroxypropyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.

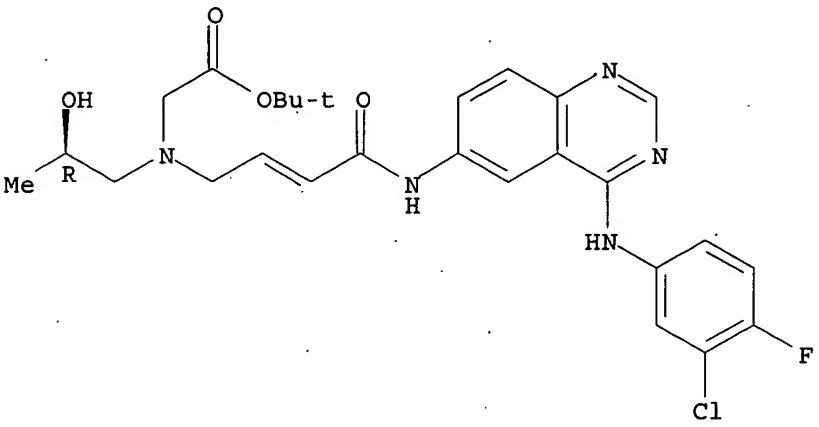


RN 402855-38-3 CAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-6-quinazolinyl]-4-(5,5-dimethyl-2-oxo-4-morpholinyl)- (9CI) (CA INDEX NAME)



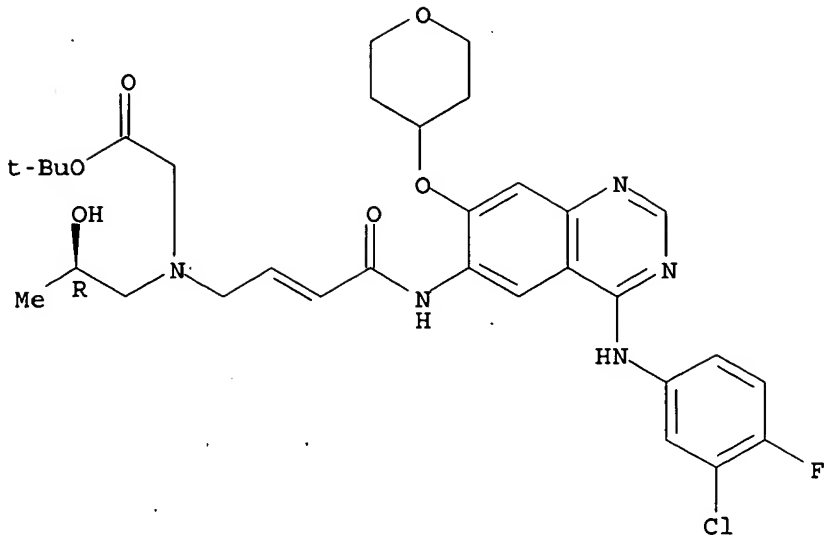
RN 402855-39-4 CAPLUS
CN Glycine, N-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-6-quinazolinyl]amino]-4-oxo-2-butenyl]-N-[(2R)-2-hydroxypropyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



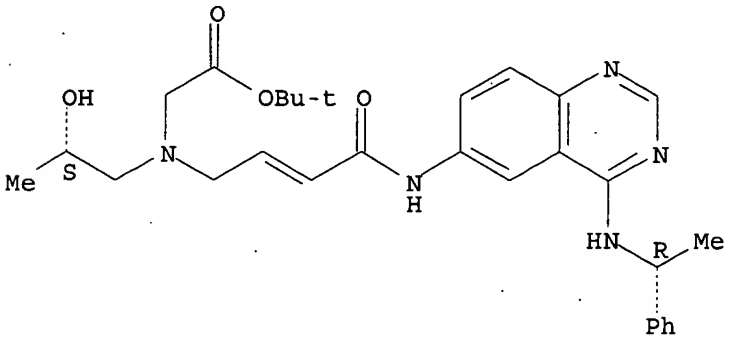
RN 402855-40-7 CAPLUS
CN Glycine, N-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-[(tetrahydro-2H-pyran-4-yl)oxy]-6-quinazolinyl]amino]-4-oxo-2-butenyl]-N-[(2R)-2-hydroxypropyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



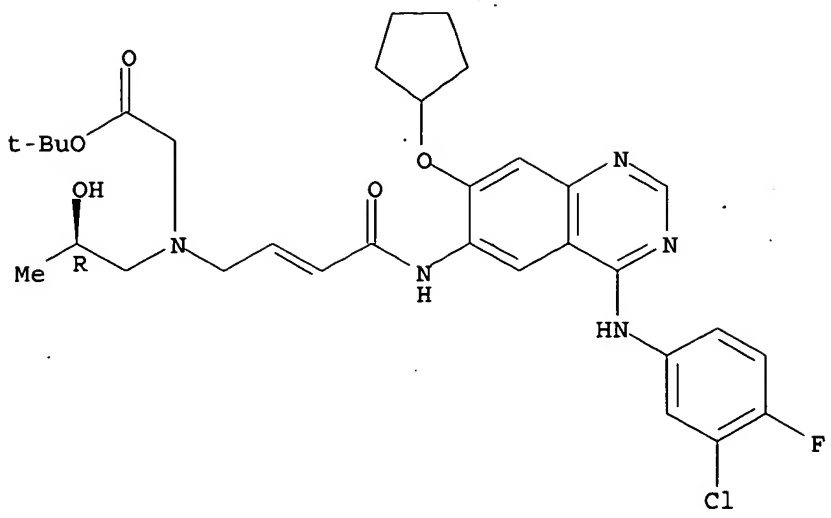
RN 402855-41-8 CAPLUS
CN Glycine, N-[(2S)-2-hydroxypropyl]-N-[4-oxo-4-[[4-[[(1R)-1-phenylethyl]amino]-6-quinazolinyl]amino]-2-butenyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



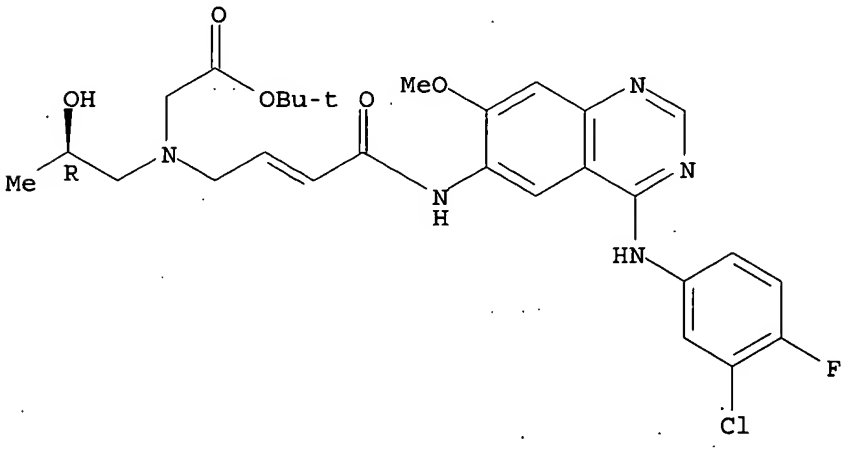
RN 402855-42-9 CAPLUS
CN Glycine, N-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopentyloxy)-6-quinazolinyl]amino]-4-oxo-2-butenyl]-N-[(2R)-2-hydroxypropyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



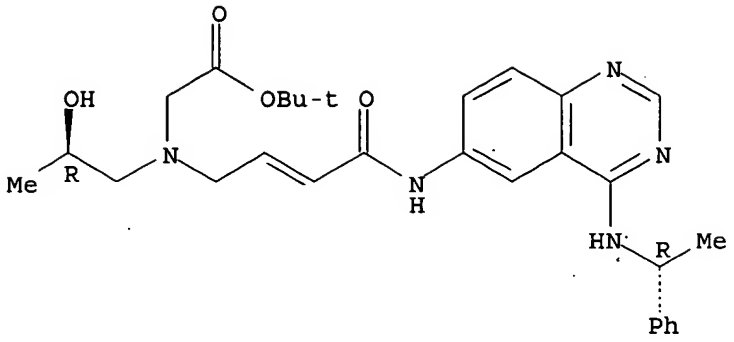
RN 402855-43-0 CAPLUS
CN Glycine, N-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-methoxy-6-quinazolinyl]amino]-4-oxo-2-butenyl]-N-[(2R)-2-hydroxypropyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



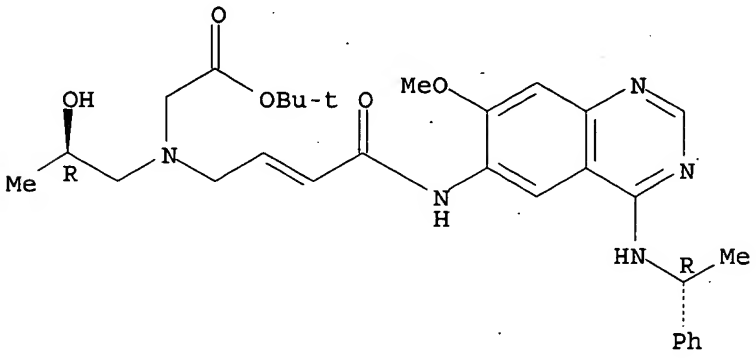
RN 402855-44-1 CAPLUS
CN Glycine, N-[(2R)-2-hydroxypropyl]-N-[4-oxo-4-[[4-[[(1R)-1-phenylethyl]amino]-6-quinazolinyl]amino]-2-butenyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



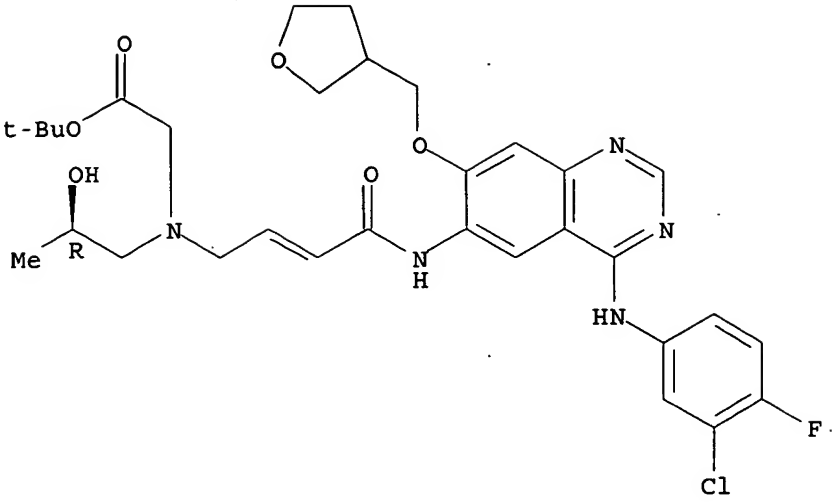
RN 402855-45-2 CAPLUS
CN Glycine, N-[(2R)-2-hydroxypropyl]-N-[4-[[7-methoxy-4-[[(1R)-1-phenylethyl]amino]-6-quinazolinyl]amino]-4-oxo-2-butenyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.

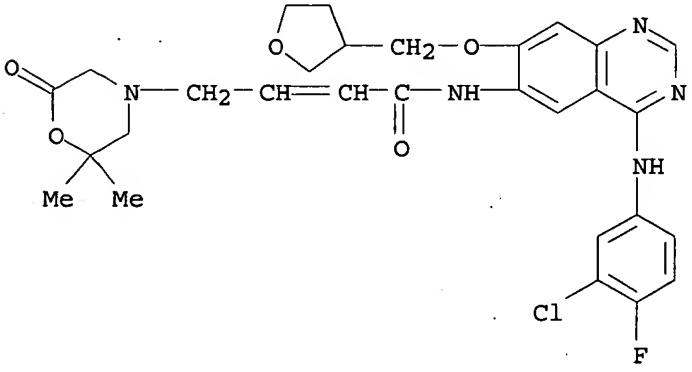


RN 402855-46-3 CAPLUS
CN Glycine, N-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-[(tetrahydro-3-furanyl)methoxy]-6-quinazolinyl]amino]-4-oxo-2-butenyl]-N-[(2R)-2-hydroxypropyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

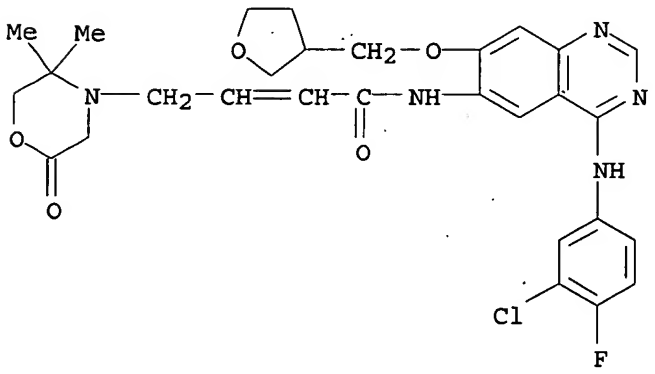
Absolute stereochemistry.
Double bond geometry unknown.



RN 402855-47-4 CAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-[(tetrahydro-3-furanyl)methoxy]-6-quinazolinyl]-4-(2,2-dimethyl-6-oxo-4-morpholinyl)-(9CI) (CA INDEX NAME)



RN 402855-48-5 CAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-[(tetrahydro-3-furanyl)methoxy]-6-quinazolinyl]-4-(5,5-dimethyl-2-oxo-4-morpholinyl)-(9CI) (CA INDEX NAME)



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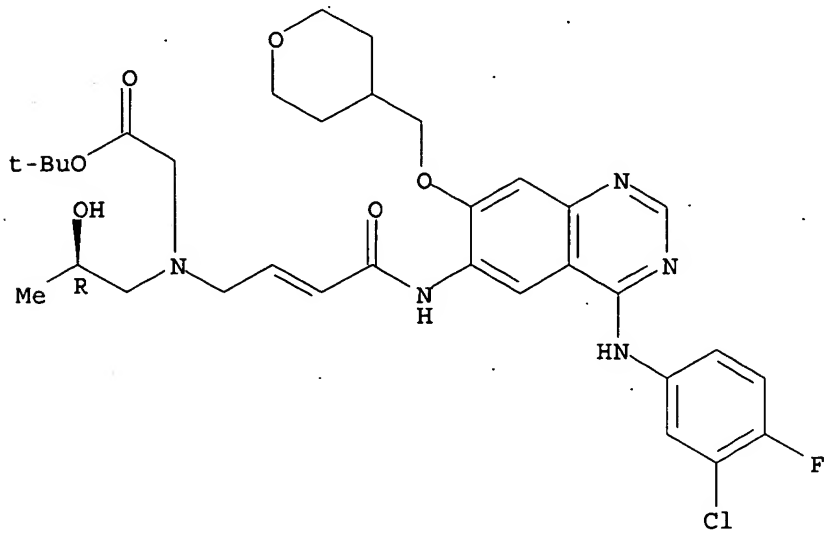
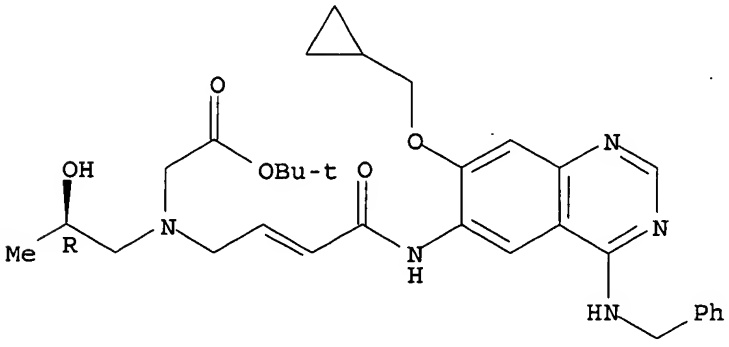
RN 402855-49-6 CAPLUS
CN Glycine, N-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-[(tetrahydro-2H-pyran-4-yl)methoxy]-6-quinazolinyl]amino]-4-oxo-2-butenyl]-N-[(2R)-2-hydroxypropyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



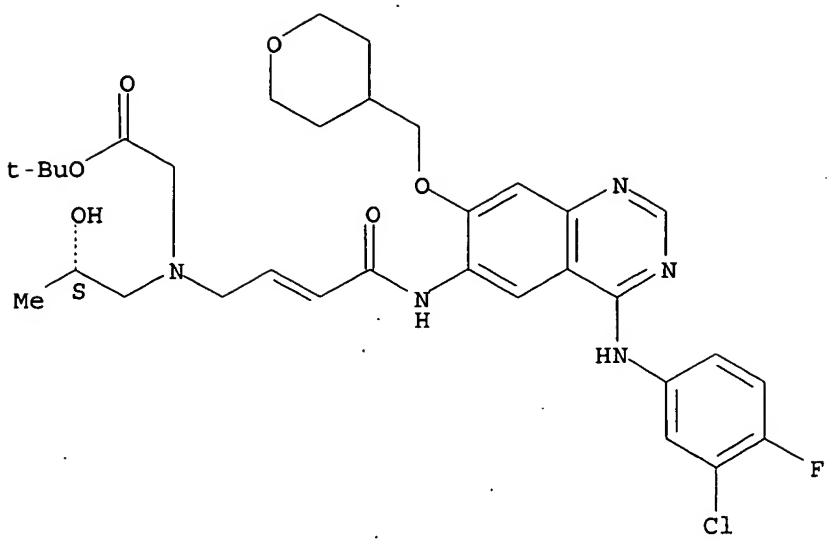
RN 402855-50-9 CAPLUS
CN Glycine, N-[4-[[7-(cyclopropylmethoxy)-4-[(phenylmethyl)amino]-6-quinazolinyl]amino]-4-oxo-2-butenyl]-N-[(2R)-2-hydroxypropyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



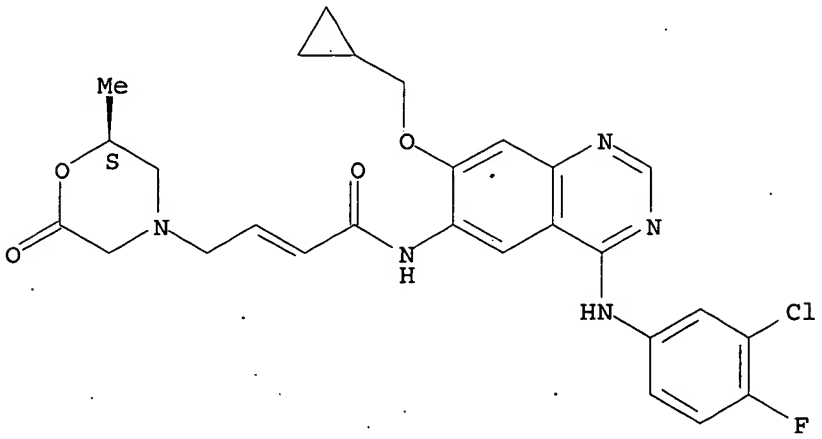
RN 402855-51-0 CAPLUS
CN Glycine, N-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-[(tetrahydro-2H-pyran-4-yl)methoxy]-6-quinazolinyl]amino]-4-oxo-2-butenyl]-N-[(2S)-2-hydroxypropyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



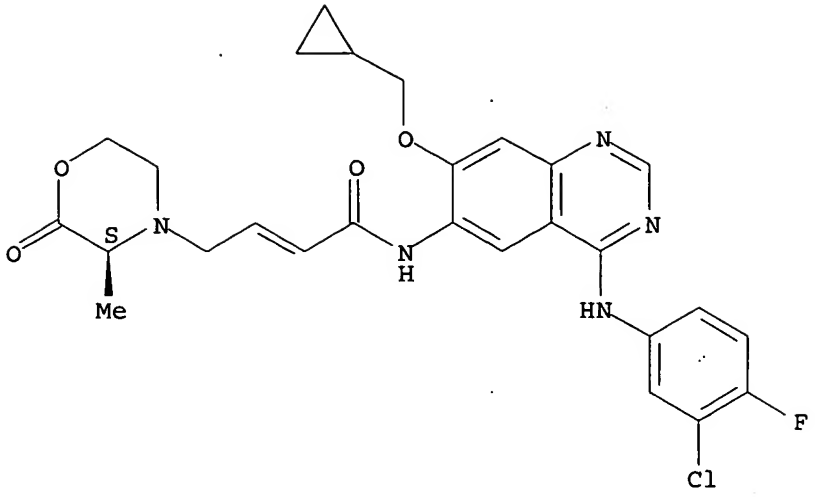
RN 402855-52-1 CAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-[(2S)-2-methyl-6-oxo-4-morpholinyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



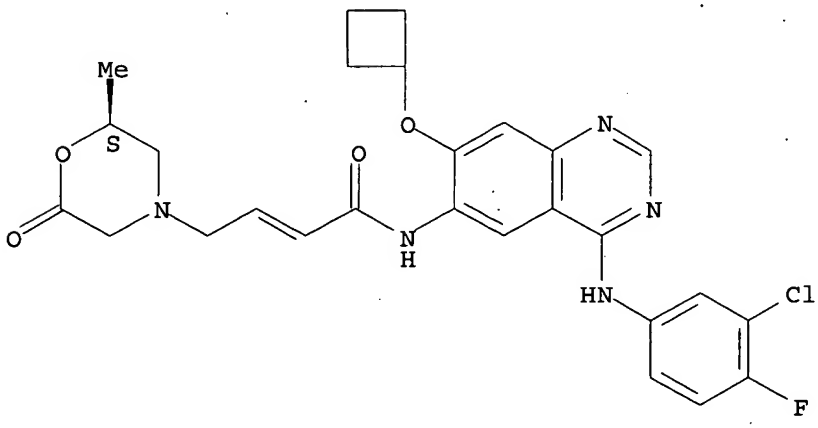
RN 402855-54-3 CAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-[(3S)-3-methyl-2-oxo-4-morpholinyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



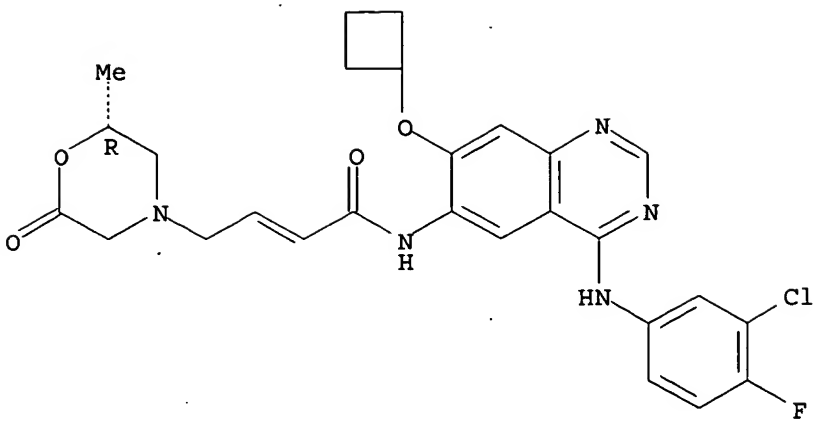
RN 402855-55-4 CAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclobutyloxy)-6-quinazolinyl]-4-[(2S)-2-methyl-6-oxo-4-morpholinyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



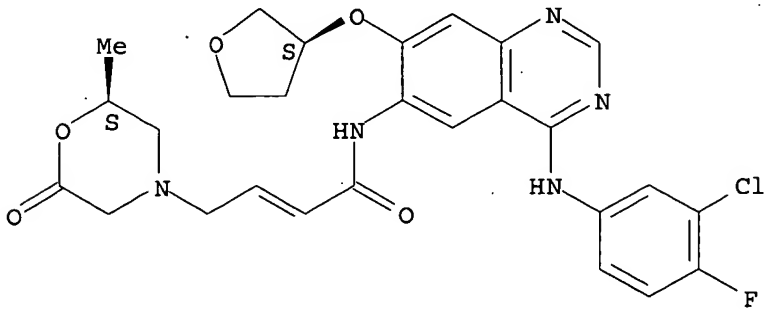
RN 402855-56-5 CAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclobutyloxy)-6-quinazolinyl]-4-[(2R)-2-methyl-6-oxo-4-morpholinyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



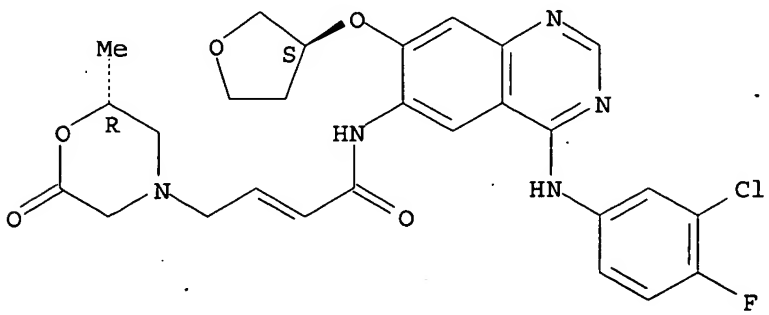
RN 402855-57-6 CAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-[[(3S)-tetrahydro-3-furanyl]oxy]-6-quinazolinyl]-4-[(2S)-2-methyl-6-oxo-4-morpholinyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



RN 402855-58-7 CAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-[[(3S)-tetrahydro-3-furanyl]oxy]-6-quinazolinyl]-4-[(2R)-2-methyl-6-oxo-4-morpholinyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



RN 402855-59-8 CAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-[[(3R)-tetrahydro-3-furanyl]oxy]-6-quinazolinyl]-4-[(2R)-2-methyl-6-oxo-4-morpholinyl]- (9CI)

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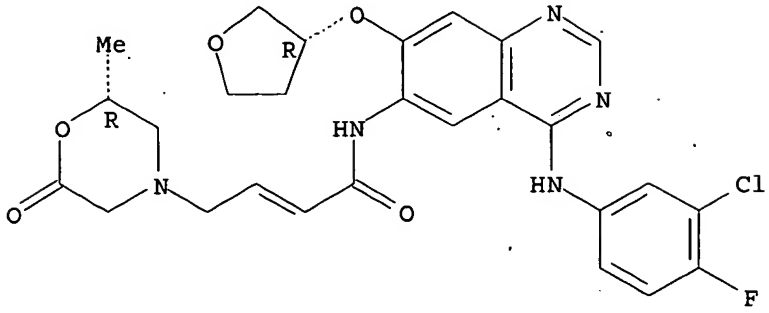
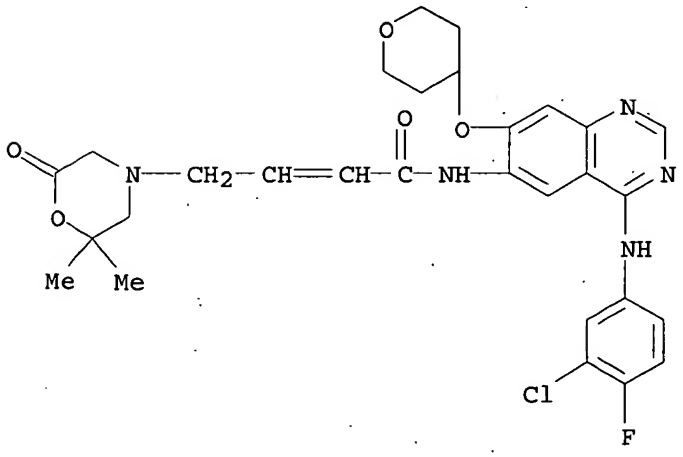
(CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.

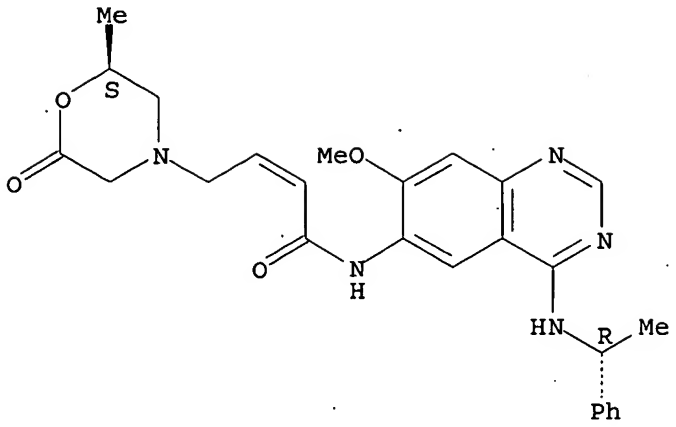


RN 402855-60-1 CAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-[(tetrahydro-2H-pyran-4-yl)oxy]-6-quinazolinyl]-4-(2,2-dimethyl-6-oxo-4-morpholinyl)- (9CI) (CA INDEX NAME)



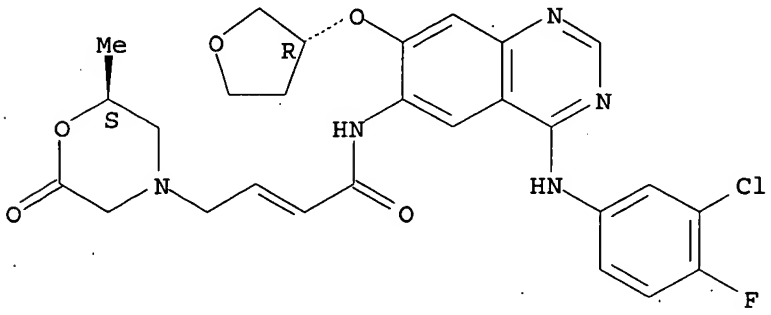
RN 402855-61-2 CAPLUS
CN 2-Butenamide, N-[7-methoxy-4-[[(1R)-1-phenylethyl]amino]-6-quinazolinyl]-4-[(2S)-2-methyl-6-oxo-4-morpholinyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



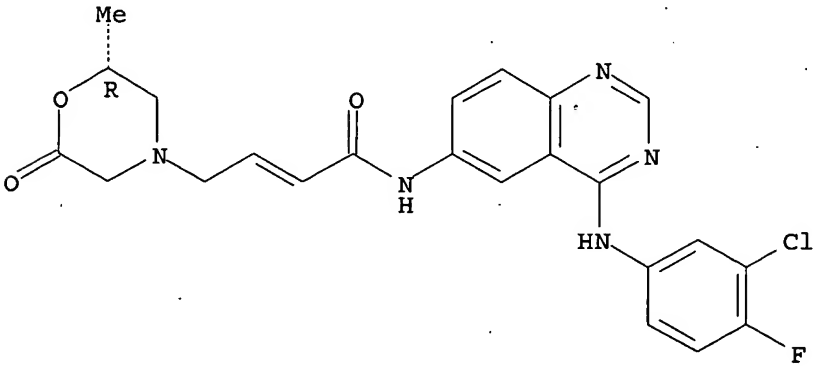
RN 402855-62-3 CAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-[[(3R)-tetrahydro-3-furanyl]oxy]-6-quinazolinyl]-4-[(2S)-2-methyl-6-oxo-4-morpholinyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



RN 402855-63-4 CAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-6-quinazolinyl]-4-[(2R)-2-methyl-6-oxo-4-morpholinyl]- (9CI) (CA INDEX NAME)

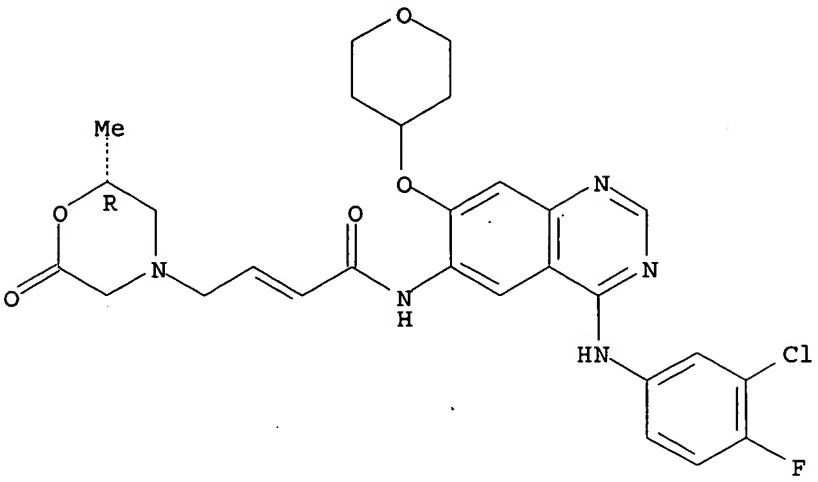
Absolute stereochemistry.
Double bond geometry unknown.



RN 402855-64-5 CAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-[(tetrahydro-2H-

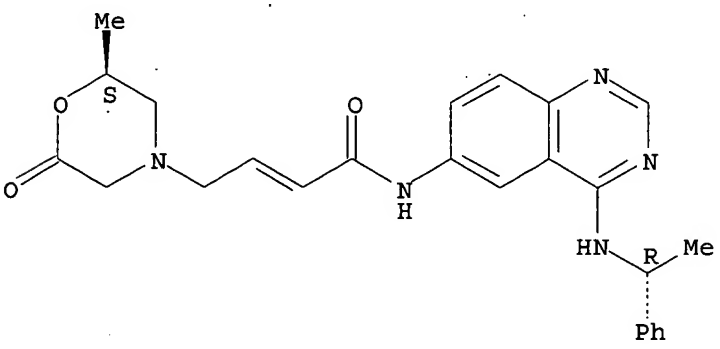
pyran-4-yl)oxy]-6-quinazolinyl]-4-[(2R)-2-methyl-6-oxo-4-morpholinyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



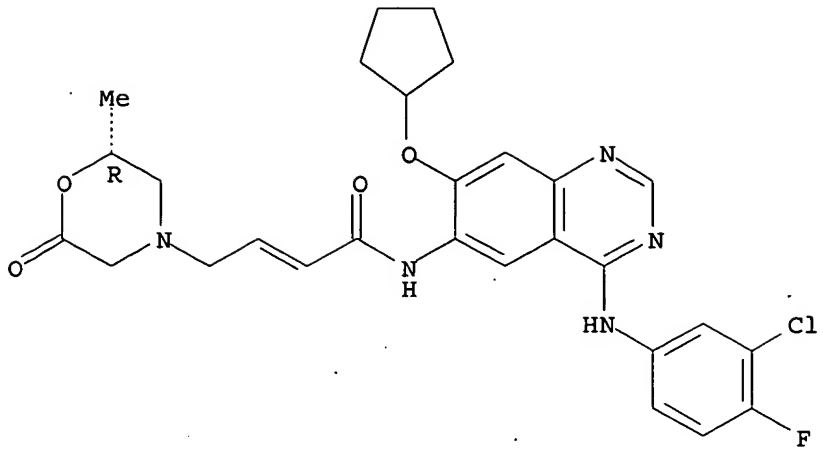
RN 402855-65-6 CAPLUS
CN 2-Butenamide, 4-[(2S)-2-methyl-6-oxo-4-morpholinyl]-N-[4-[[(1R)-1-phenylethyl]amino]-6-quinazolinyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



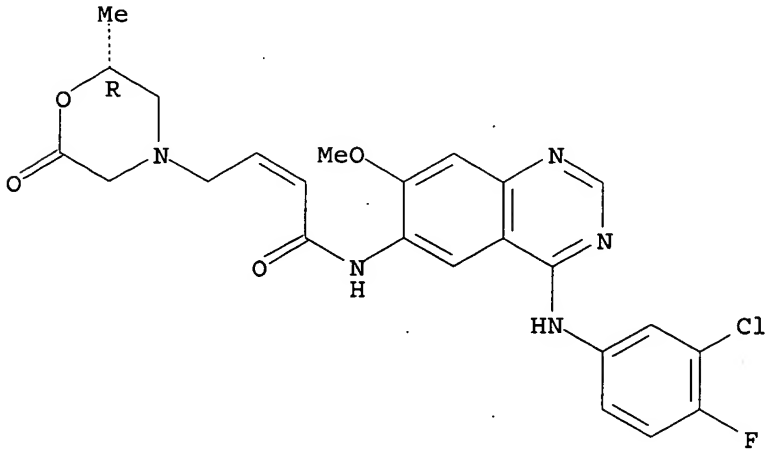
RN 402855-66-7 CAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopentyloxy)-6-quinazolinyl]-4-[(2R)-2-methyl-6-oxo-4-morpholinyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



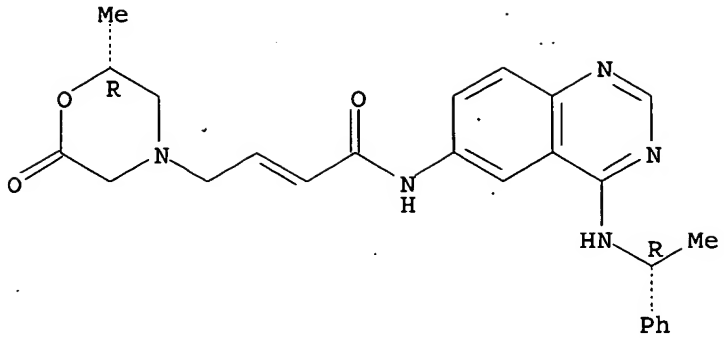
RN 402855-67-8 CAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-methoxy-6-quinazolinyl]-4-[(2R)-2-methyl-6-oxo-4-morpholinyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



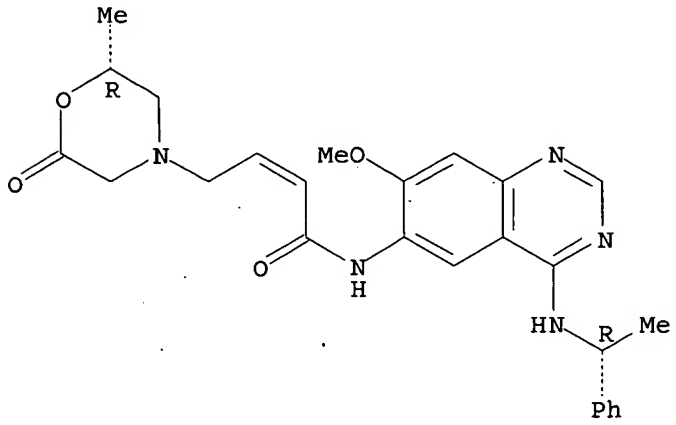
RN 402855-68-9 CAPLUS
CN 2-Butenamide, 4-[(2R)-2-methyl-6-oxo-4-morpholinyl]-N-[4-[[(1R)-1-phenylethyl]amino]-6-quinazolinyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



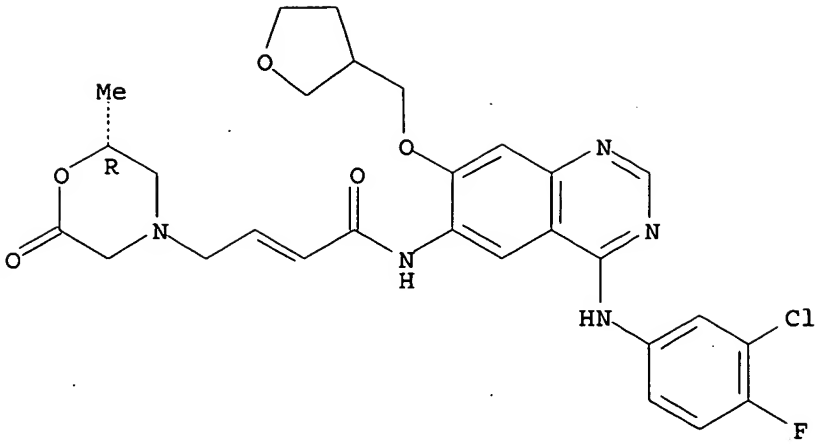
RN 402855-69-0 CAPLUS
CN 2-Butenamide, N-[7-methoxy-4-[[(1R)-1-phenylethyl]amino]-6-quinazolinyl]-4-[(2R)-2-methyl-6-oxo-4-morpholinyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



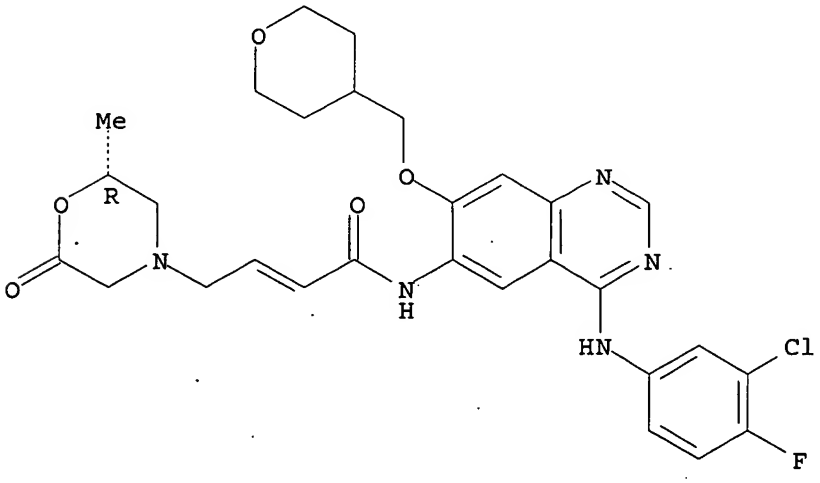
RN 402855-70-3 CAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-[(tetrahydro-3-furanyl)methoxy]-6-quinazolinyl]-4-[(2R)-2-methyl-6-oxo-4-morpholinyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



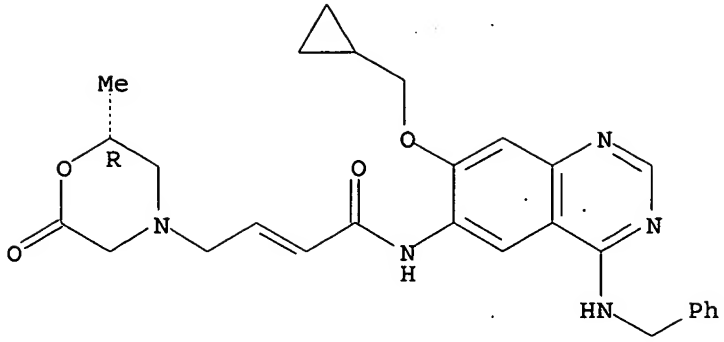
RN 402855-71-4 CAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-[(tetrahydro-2H-pyran-4-yl)methoxy]-6-quinazolinyl]-4-[(2R)-2-methyl-6-oxo-4-morpholinyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



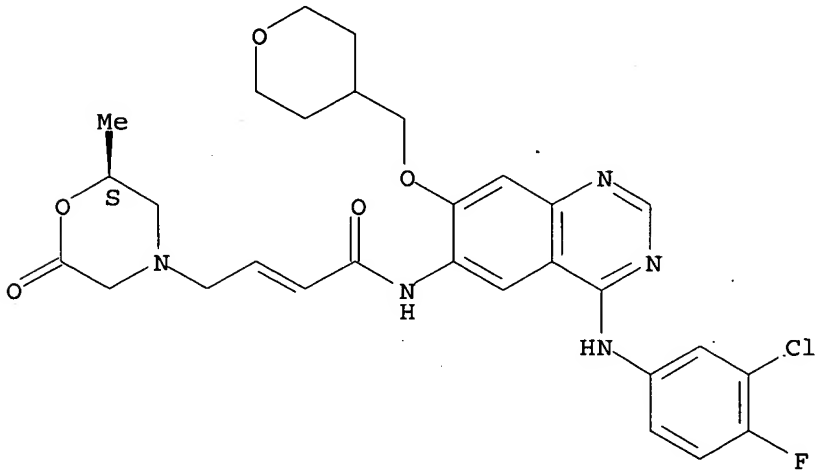
RN 402855-72-5 CAPLUS
CN 2-Butenamide, N-[7-(cyclopropylmethoxy)-4-[(phenylmethyl)amino]-6-quinazolinyl]-4-[(2R)-2-methyl-6-oxo-4-morpholinyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



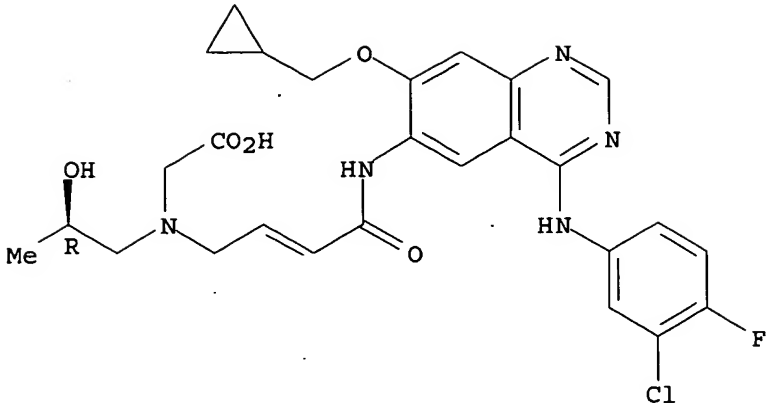
RN 402855-73-6 CAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-[(tetrahydro-2H-pyran-4-yl)methoxy]-6-quinazolinyl]-4-[(2S)-2-methyl-6-oxo-4-morpholinyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.

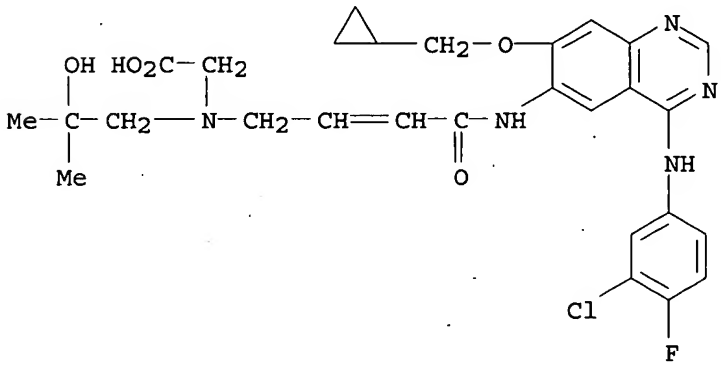


RN 402855-74-7 CAPLUS
CN Glycine, N-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]amino]-4-oxo-2-butenyl]-N-[(2R)-2-hydroxypropyl]- (9CI) (CA INDEX NAME)

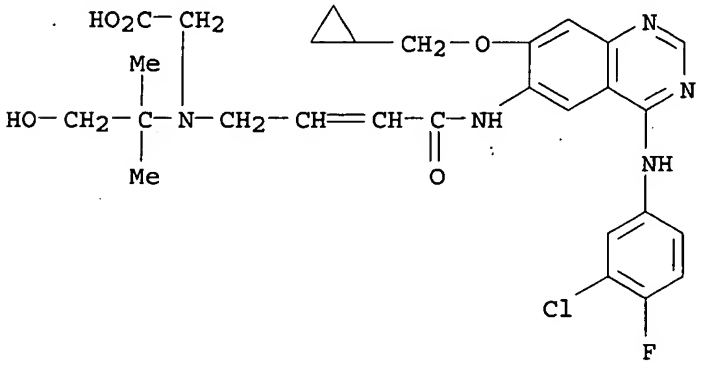
Absolute stereochemistry.
Double bond geometry unknown.



RN 402855-75-8 CAPLUS
CN Glycine, N-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]amino]-4-oxo-2-butenyl]-N-(2-hydroxy-2-methylpropyl)- (9CI) (CA INDEX NAME)



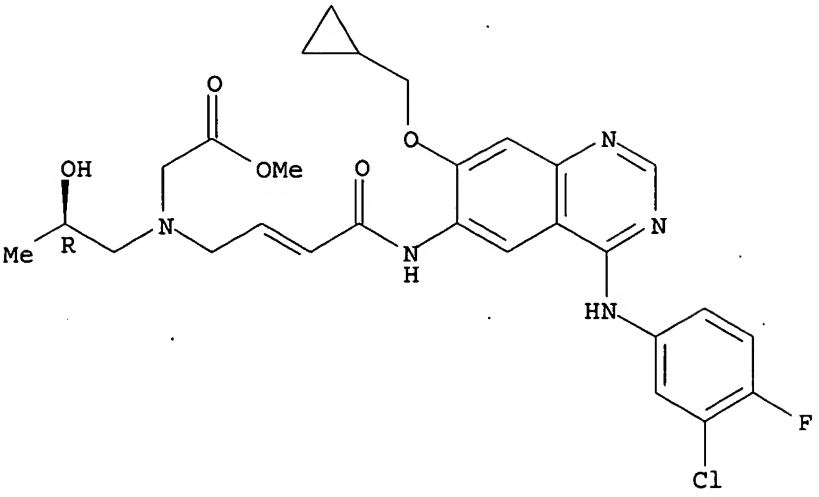
RN 402855-76-9 CAPLUS
CN Glycine, N-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]amino]-4-oxo-2-butenyl]-N-(2-hydroxy-1,1-dimethylethyl)-(9CI) (CA INDEX NAME)



RN 402855-77-0 CAPLUS
CN Glycine, N-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]amino]-4-oxo-2-butenyl]-N-[(2R)-2-hydroxypropyl]-, methyl

ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

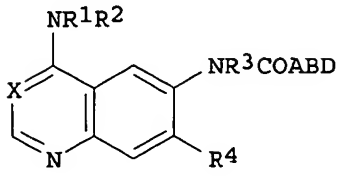
L3 ANSWER 4 OF 13 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2001:762992 CAPLUS
DOCUMENT NUMBER: 135:303907
TITLE: Preparation of quinazolines as inhibitors of epidermal growth factor-mediated signal transduction.
INVENTOR(S): Himmelsbach, Frank; Langkopf, Elke; Jung, Birgit; Blech, Stefan; Solca, Flavio
PATENT ASSIGNEE(S): Boehringer Ingelheim Pharma K.-G., Germany
SOURCE: PCT Int. Appl., 95 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001077104	A1	20011018	WO 2001-EP3694	20010331
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
DE 10017539	A1	20011011	DE 2000-10017539	20000408
DE 10040525	A1	20020228	DE 2000-10040525	20000818
EP 1280798	A1	20030205	EP 2001-938076	20010331
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				

PRIORITY APPLN. INFO.: DE 2000-10017539 A 20000408
DE 2000-10040525 A 20000818
WO 2001-EP3694 W 20010331

10/ 023,099

OTHER SOURCE(S): MARPAT 135:303907
GI

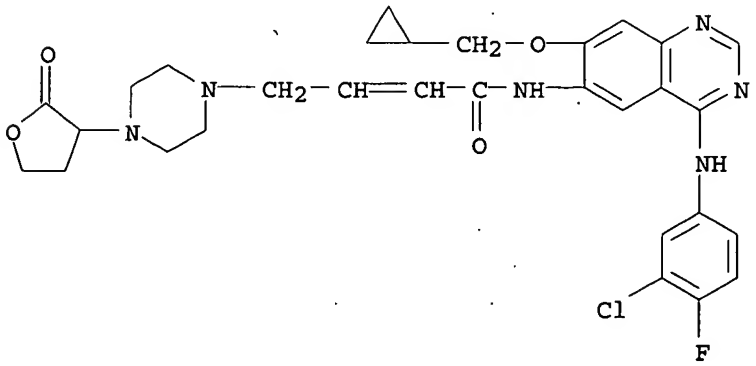


I

AB Title compds. [I; X = NCN, N; R1 = H, alkyl; R2 = (substituted) Ph, PhCH2, PhCH2CH2; R3 = H, alkyl; R4 = H, alkoxy, cycloalkoxy, cycloalkylalkoxy; A = (substituted) vinylene; B = bond, (fluoro)alkylene; D = substituted pyrrolidinyl, piperidinyl, piperazinyl, etc.], were prepd. Thus, 4-[(3-chloro-4-fluorophenyl)amino]-6-[[4-(piperazin-1-yl)-1-oxo-2-buten-1-yl]amino]-7-cyclopropylmethoxyquinazoline (prepn. given) in THF was treated with Et3N and then with 3-bromodihydrofuran-2-one in THF under ice cooling followed by stirring for 48 h at room temp. to give 56% 4-[(3-chloro-4-fluorophenyl)amino]-6-[[4-[4-(2-oxotetrahydrofuran-3-yl)piperazin-1-yl]-1-oxo-2-buten-1-yl]amino]-7-cyclopropylmethoxyquinazoline. The latter inhibited epidermal growth factor (EGF)-dependent proliferation of F/L-HERc cells with IC50 = 0.05 nM.

IT **365532-35-0P 365532-36-1P 365532-37-2P**
365532-39-4P 365532-41-8P 365532-42-9P
365532-44-1P 365532-45-2P 365532-46-3P
365532-47-4P 365532-48-5P 365532-49-6P
367282-07-3P 367282-12-0P 367282-15-3P
367282-23-3P 367282-25-5P 367282-27-7P
367282-29-9P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of quinazolines as inhibitors of epidermal growth factor-mediated signal transduction)

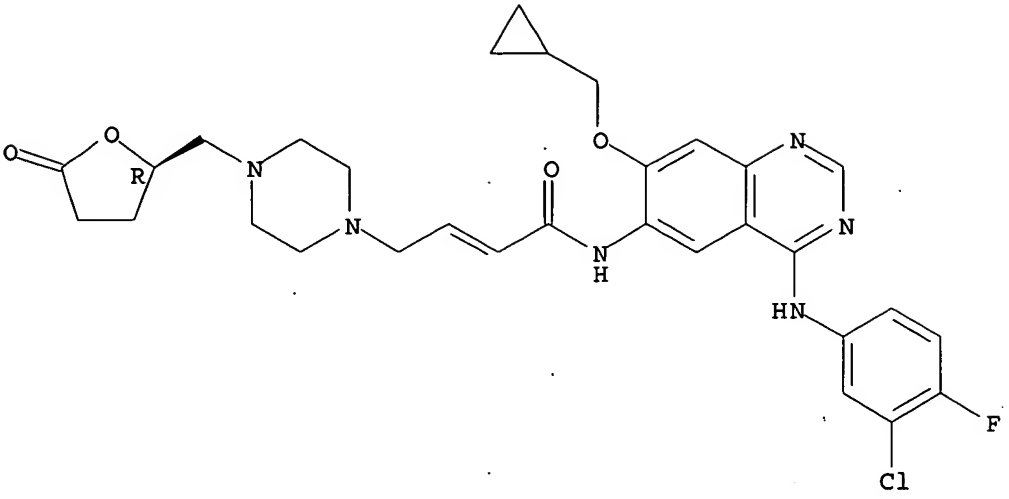
RN 365532-35-0 CAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-[4-(tetrahydro-2-oxo-3-furanyl)-1-piperazinyl]- (9CI) (CA INDEX NAME)



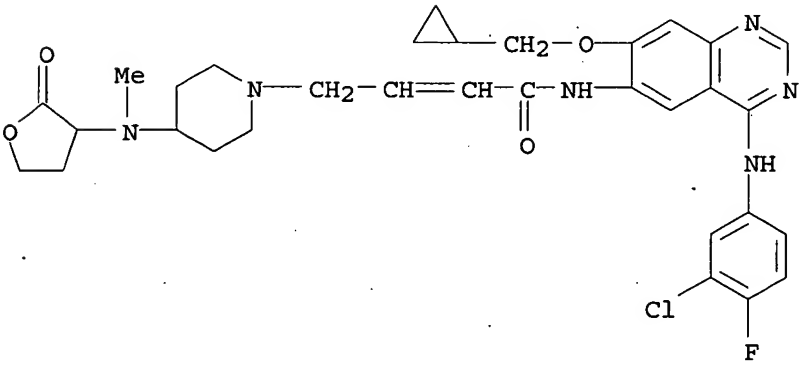
RN 365532-36-1 CAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-[4-[[(2R)-tetrahydro-5-oxo-2-furanyl]methyl]-1-piperazinyl]- (9CI) (CA INDEX NAME)

10/ 023,099

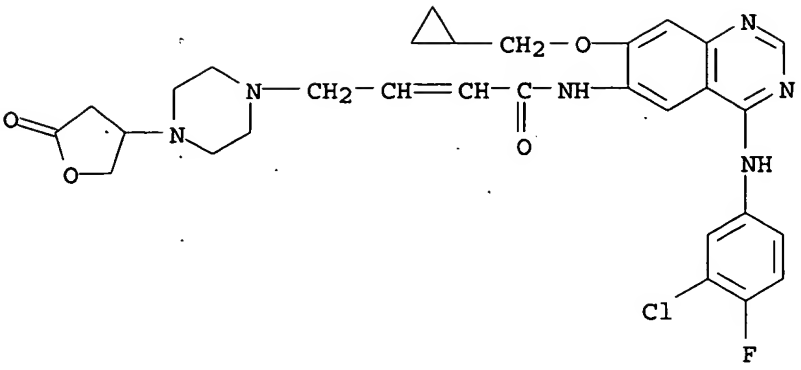
Absolute stereochemistry.
Double bond geometry unknown.



RN 365532-37-2 CAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-[4-[methyl(tetrahydro-2-oxo-3-furanyl)amino]-1-piperidinyl]- (9CI) (CA INDEX NAME)

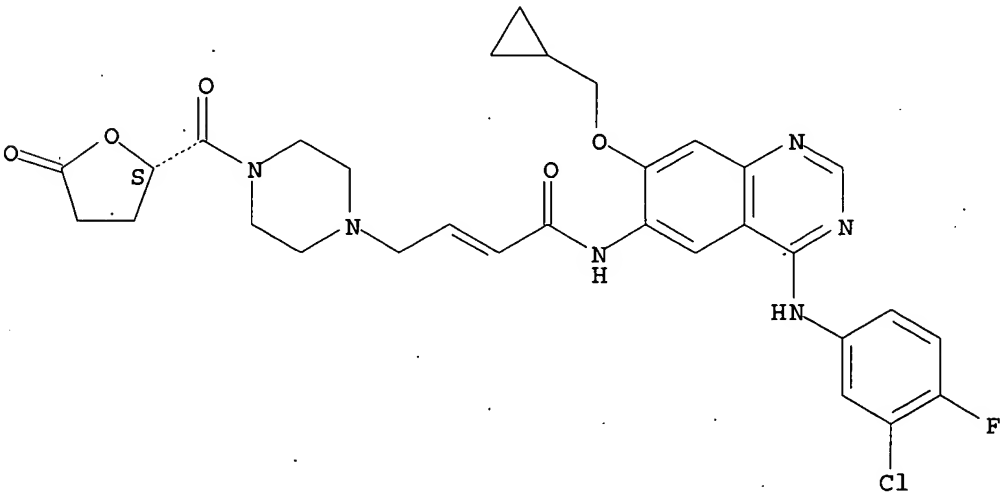


RN 365532-39-4 CAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-[4-(tetrahydro-5-oxo-3-furanyl)-1-piperazinyl]- (9CI) (CA INDEX NAME)

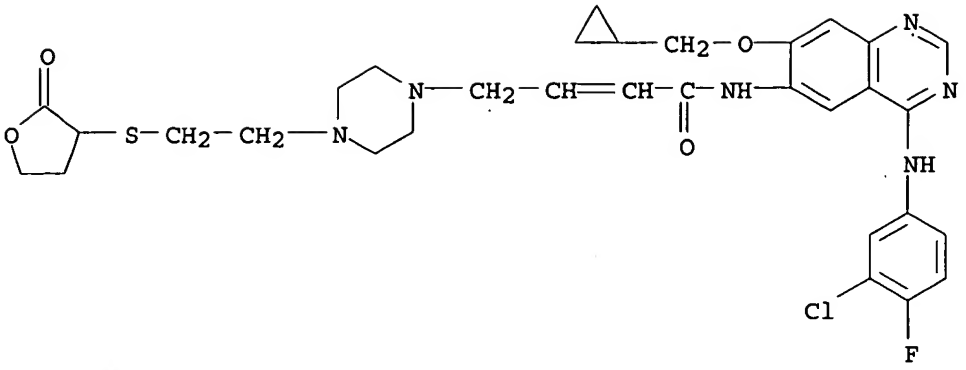


RN 365532-41-8 CAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-[4-[[(2S)-tetrahydro-5-oxo-2-furanyl]carbonyl]-1-piperazinyl]- (9CI) (CA INDEX NAME)

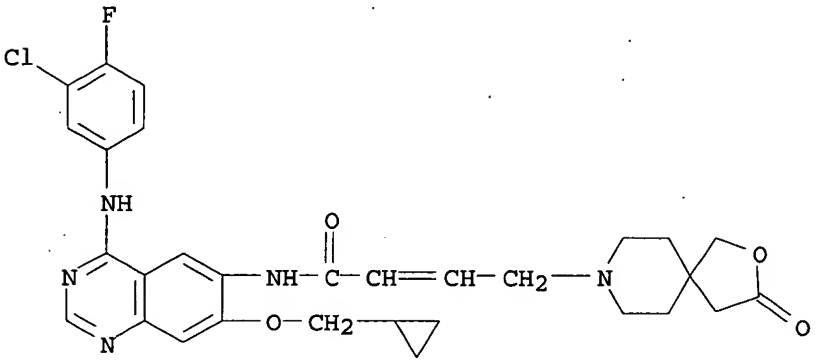
Absolute stereochemistry.
Double bond geometry unknown.



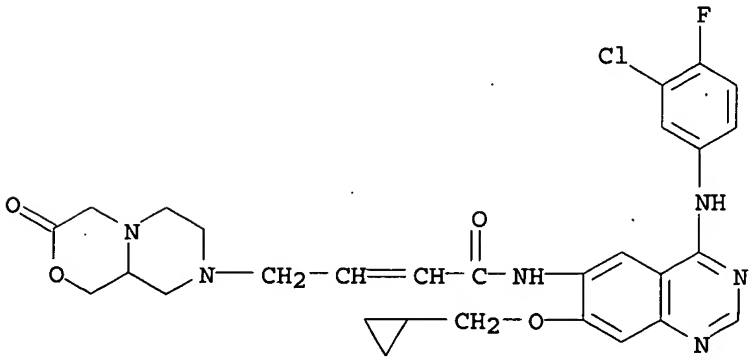
RN 365532-42-9 CAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-[4-[2-[(tetrahydro-2-oxo-3-furanyl)thio]ethyl]-1-piperazinyl]- (9CI) (CA INDEX NAME)



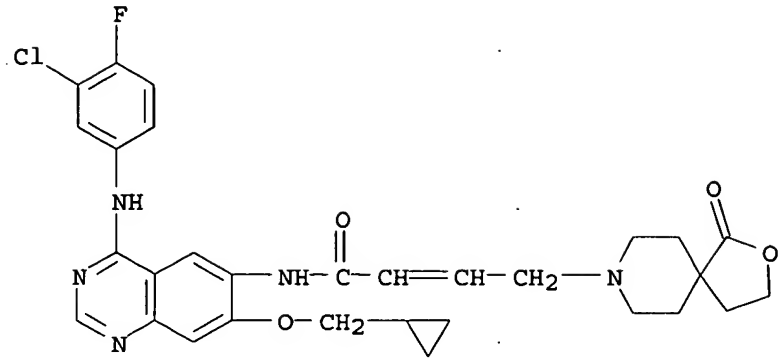
RN 365532-44-1 CAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-(3-oxo-2-oxa-8-azaspiro[4.5]dec-8-yl)- (9CI) (CA INDEX NAME)



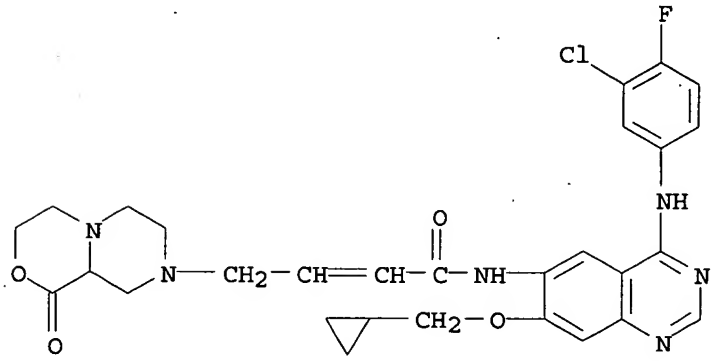
RN 365532-45-2 CAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-(hexahydro-3-oxopyrazino[2,1-c][1,4]oxazin-8(1H)-yl)- (9CI) (CA INDEX NAME)



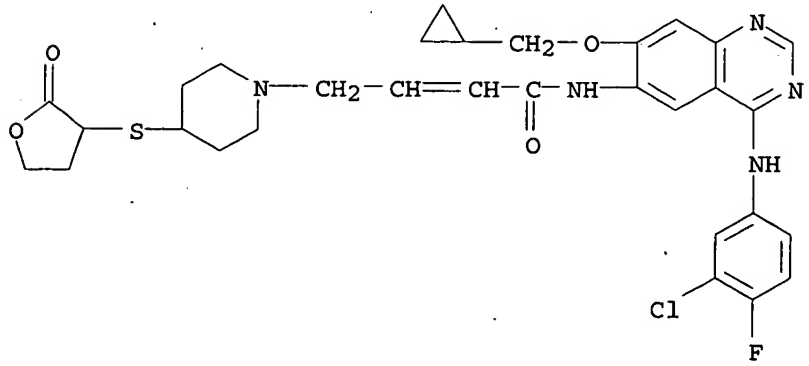
RN 365532-46-3 CAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-(1-oxo-2-oxa-8-azaspiro[4.5]dec-8-yl)- (9CI) (CA INDEX NAME)



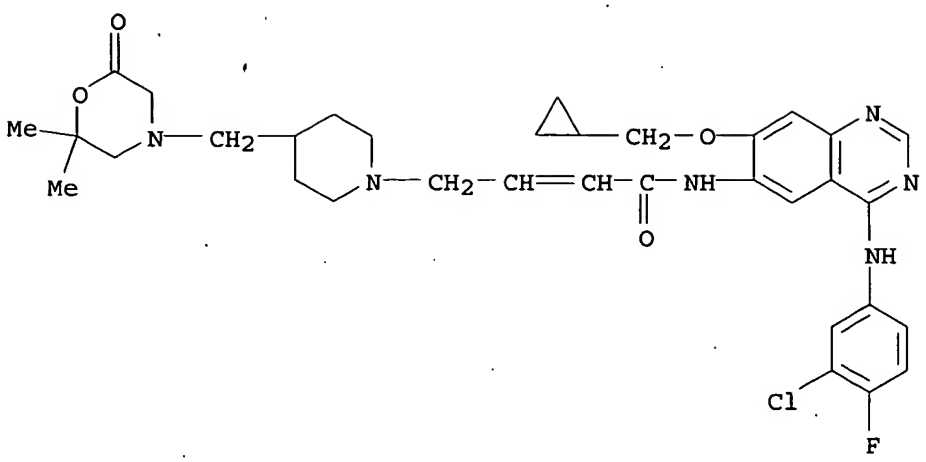
RN 365532-47-4 CAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-(hexahydro-1-oxopyrazino[2,1-c][1,4]oxazin-8(1H)-yl)- (9CI) (CA INDEX NAME)



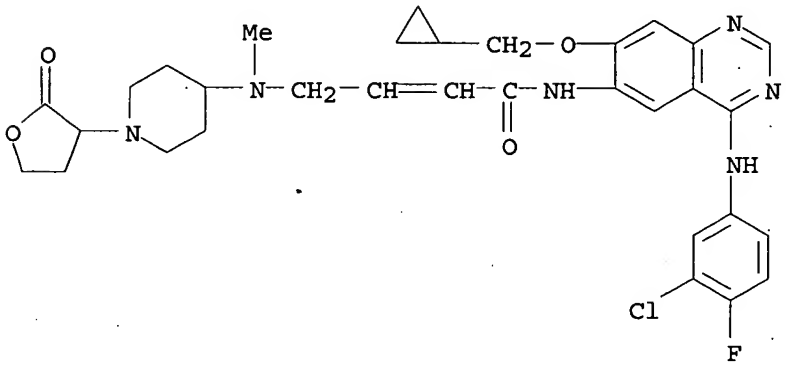
RN 365532-48-5 CAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-[4-[(tetrahydro-2-oxo-3-furanyl)thio]-1-piperidinyl]- (9CI) (CA INDEX NAME)



RN 365532-49-6 CAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-[4-[(2,2-dimethyl-6-oxo-4-morpholinyl)methyl]-1-piperidinyl]- (9CI) (CA INDEX NAME)



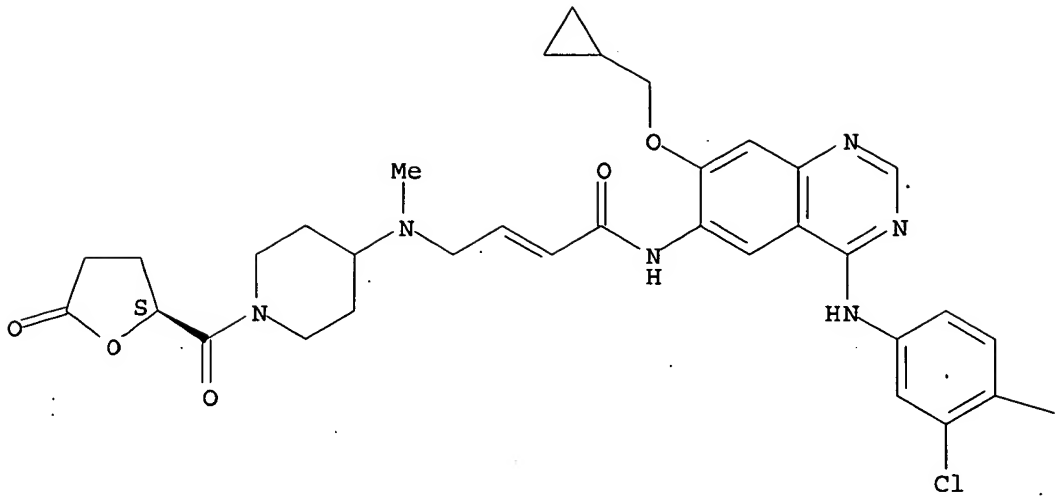
RN 367282-07-3 CAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-[methyl[1-(tetrahydro-2-oxo-3-furanyl)-4-piperidinyl]amino]- (9CI) (CA INDEX NAME)



RN 367282-12-0 CAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-[methyl[1-[[(2S)-tetrahydro-5-oxo-2-furanyl]carbonyl]-4-piperidinyl]amino]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.

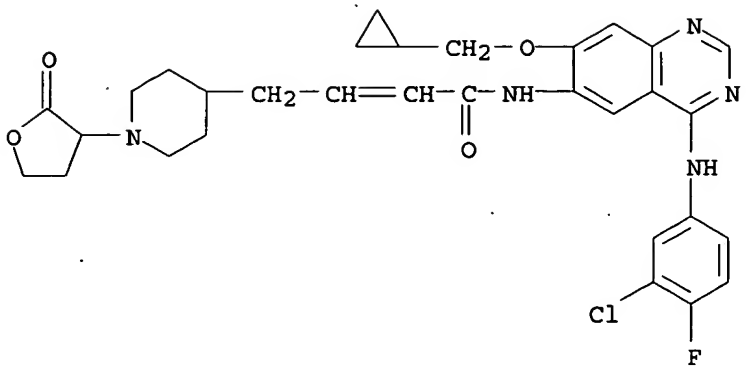
PAGE 1-A



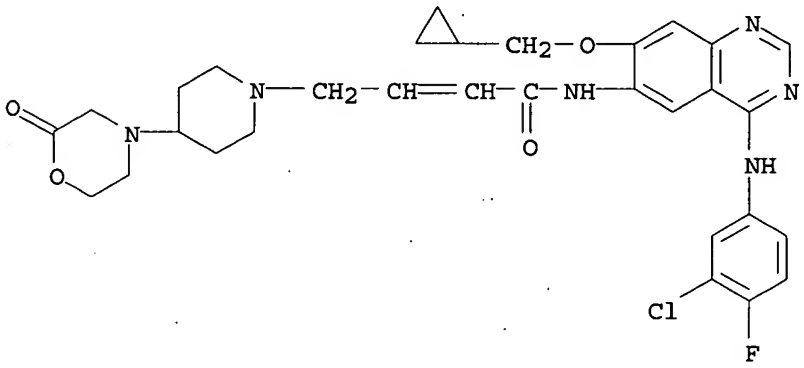
PAGE 1-B

F

RN 367282-15-3 CAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-[1-(tetrahydro-2-oxo-3-furanyl)-4-piperidinyl]- (9CI) (CA INDEX NAME)

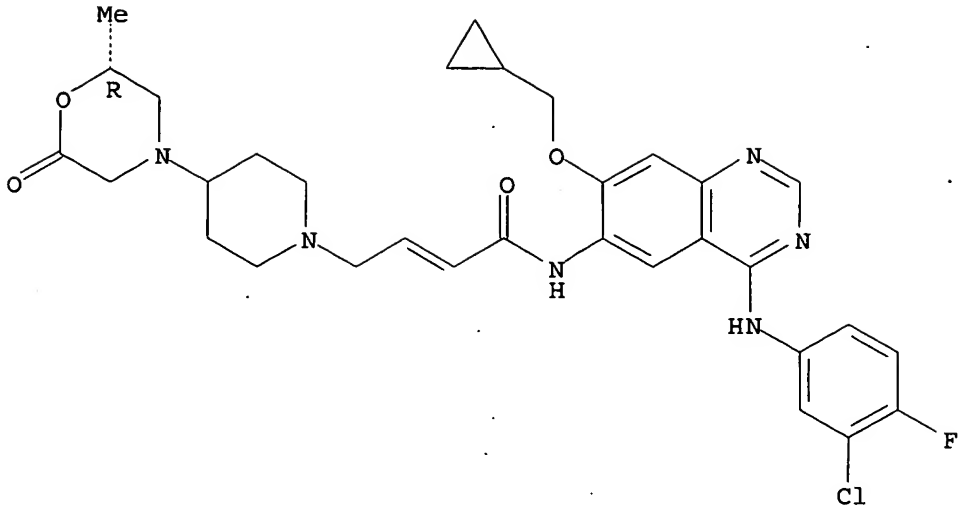


RN 367282-23-3 CAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-[4-(2-oxo-4-morpholinyl)-1-piperidinyl]- (9CI) (CA INDEX NAME)

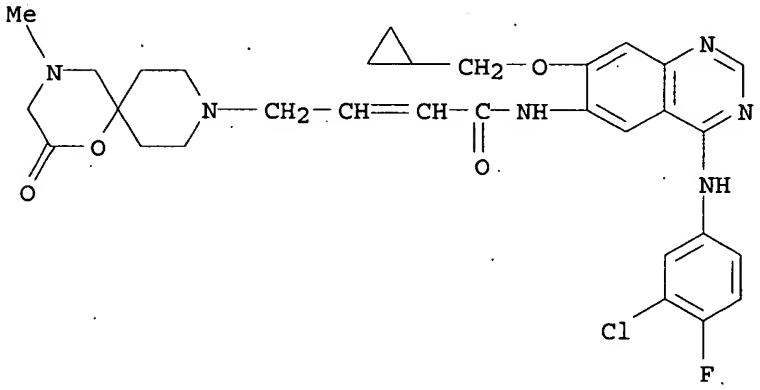


RN 367282-25-5 CAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-[4-[(2R)-2-methyl-6-oxo-4-morpholinyl]-1-piperidinyl]- (9CI) (CA INDEX NAME)

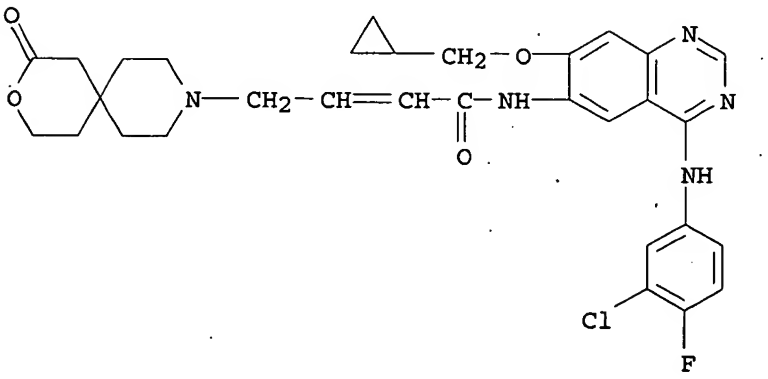
Absolute stereochemistry.
Double bond geometry unknown.



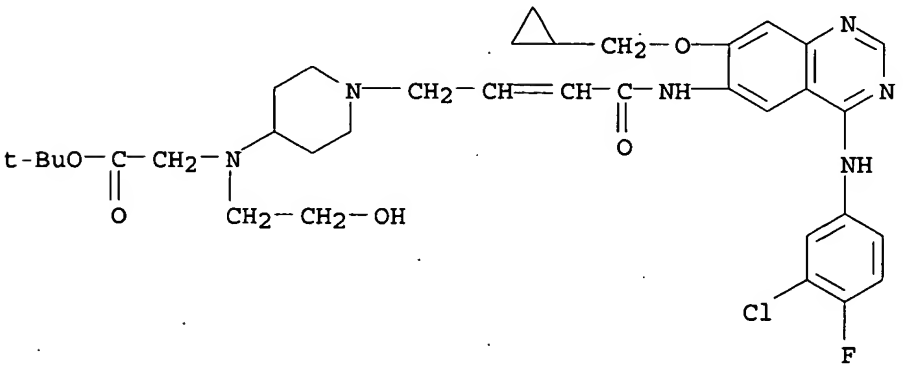
RN 367282-27-7 CAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-(4-methyl-2-oxo-1-oxa-4,9-diazaspiro[5.5]undec-9-yl)-(9CI) (CA INDEX NAME)



RN 367282-29-9 CAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-(2-oxo-3-oxa-9-azaspiro[5.5]undec-9-yl)- (9CI) (CA INDEX NAME)

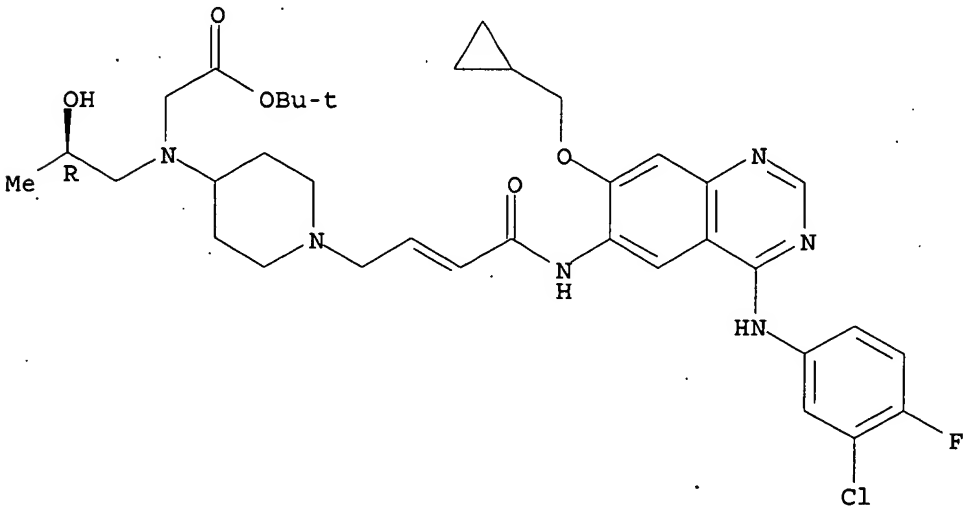


IT **367283-05-4 367283-07-6**
RL: RCT (Reactant); RACT (Reactant or reagent)
(prepn. of quinazolines as inhibitors of epidermal growth factor-mediated signal transduction)
RN 367283-05-4 CAPLUS
CN Glycine, N-[1-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]amino]-4-oxo-2-butenyl]-4-piperidinyl]-N-(2-hydroxyethyl)-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

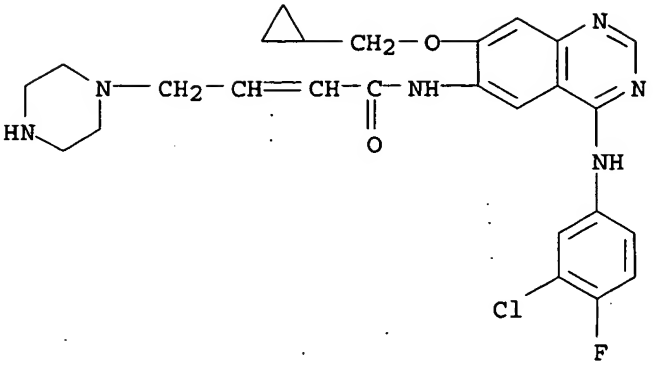


RN 367283-07-6 CAPLUS
CN Glycine, N-[1-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]amino]-4-oxo-2-butenyl]-4-piperidinyl]-N-[(2R)-2-hydroxypropyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

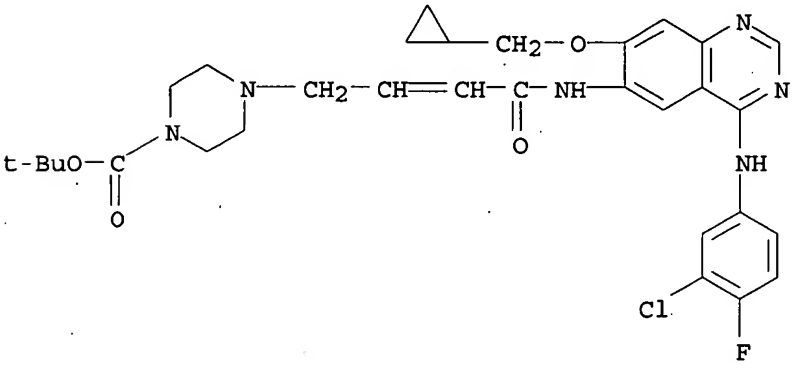
Absolute stereochemistry.
Double bond geometry unknown.



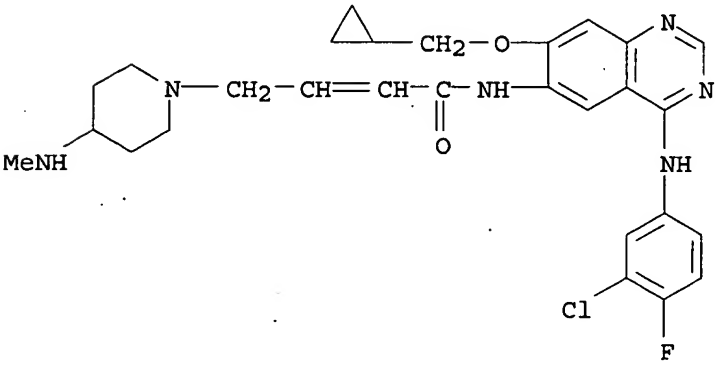
IT **290303-47-8P 290304-01-7P 365532-06-5P 365532-18-9P 367282-36-8P 367282-44-8P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of quinazolines as inhibitors of epidermal growth factor-mediated signal transduction)
RN 290303-47-8 CAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-(1-piperazinyl)- (9CI) (CA INDEX NAME)



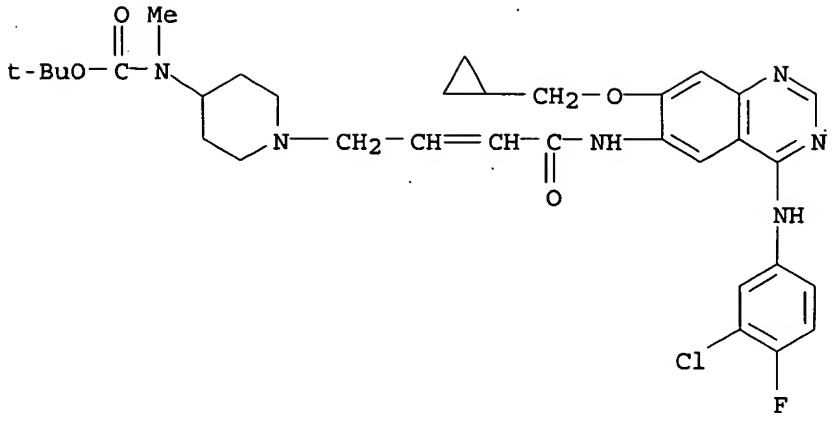
RN 290304-01-7 CAPLUS
CN 1-Piperazinecarboxylic acid, 4-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]amino]-4-oxo-2-butenyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



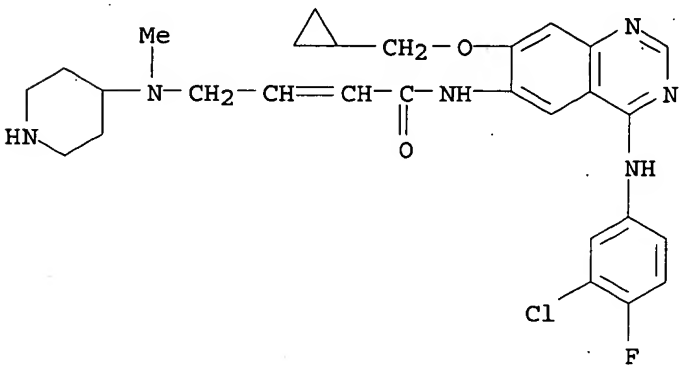
RN 365532-06-5 CAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-[4-(methylamino)-1-piperidinyl]- (9CI) (CA INDEX NAME)



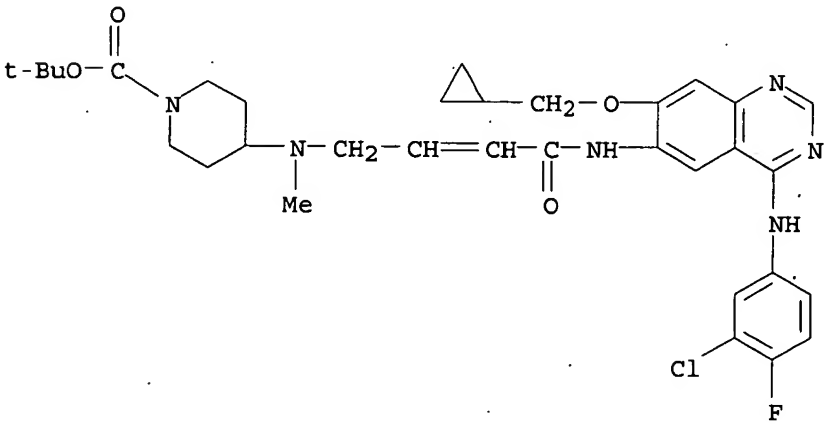
RN 365532-18-9 CAPLUS
CN Carbamic acid, [1-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]amino]-4-oxo-2-butenyl]-4-piperidinyl]methyl-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



RN 367282-36-8 CAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-(methyl-4-piperidinylamino)- (9CI) (CA INDEX NAME)



RN 367282-44-8 CAPLUS
CN 1-Piperidinecarboxylic acid, 4-[[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]amino]-4-oxo-2-butenyl]methylamino]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

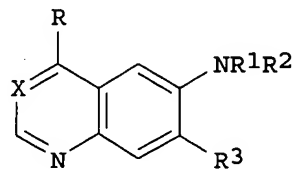


REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 5 OF 13 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2001:747043 CAPLUS
DOCUMENT NUMBER: 135:303901
TITLE: Bicyclic heterocycles as inhibitors of epidermal growth factor receptor mediated signal transduction
INVENTOR(S): Himmelsbach, Frank; Langkopf, Elke; Jung, Birgit; Blech, Stefan; Solca, Flavio
PATENT ASSIGNEE(S): Boehringer Ingelheim Pharma KG, Germany
SOURCE: Ger. Offen., 28 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 10017539	A1	20011011	DE 2000-10017539	20000408
US 2001044435	A1	20011122	US 2001-816003	20010323
WO 2001077104	A1	20011018	WO 2001-EP3694	20010331
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1280798	A1	20030205	EP 2001-938076	20010331
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				

PRIORITY APPLN. INFO.: DE 2000-10017539 A 20000408
DE 2000-10040525 A 20000818
WO 2001-EP3694 W 20010331
OTHER SOURCE(S): MARPAT 135:303901
GI



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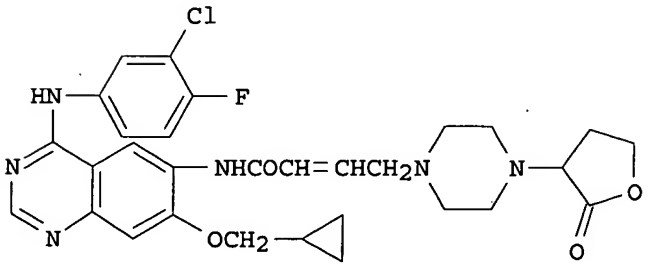


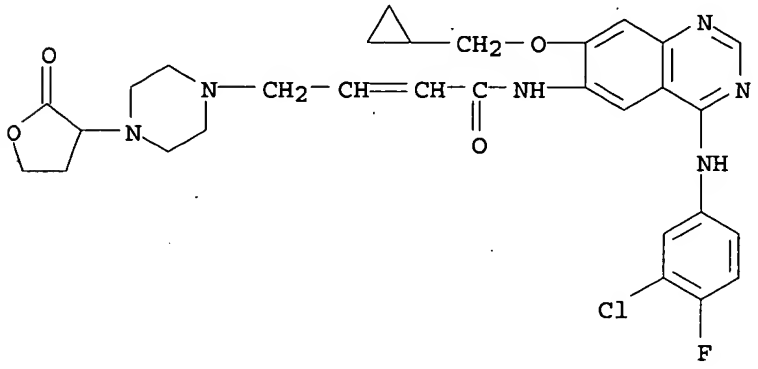
II

AB Bicyclic heterocycles I [X = N, CCN; R = substituted NH2; R1 = H, alkyl; R2 = acyl; R3 = H, (un)substituted alkoxy, cycloalkoxy,

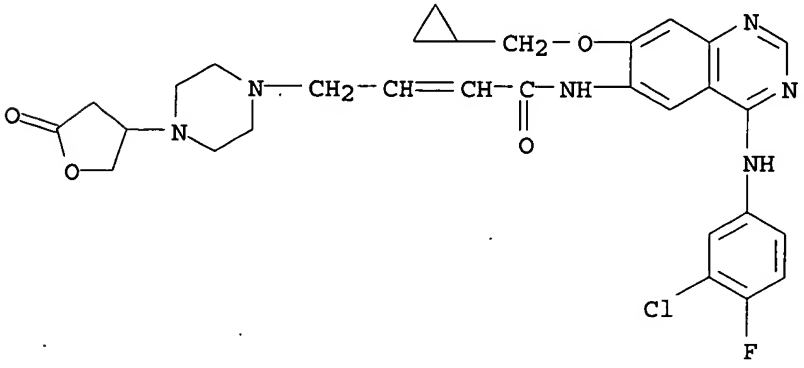
tetrahydrofuranyloxy, tetrahydropyranyloxy, tetrahydrofuranylmethoxy, tetrahydropyranylmethoxy] were prepd. for use as inhibitors of tyrosine kinase-mediated signal transduction for treatment of tumors and diseases of the lung and airway. Thus, 4-[(3-chloro-4-fluorophenyl)amino]-7-fluoro-6-nitroquinazoline was treated with cyclopropylmethanol, followed by redn. to the amine, reaction with 4-bromocrotonic acid and N-tert.-butoxycarbonylpiperazine, and deblocking to give the quinazoline II. II had an IC50 for inhibition of epidermal growth factor dependent proliferation of 0.05 nM.

IT **365532-35-0P 365532-39-4P 365532-42-9P 365532-45-2P 365532-47-4P 365532-48-5P 365532-49-6P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of bicyclic heterocycles as inhibitors of epidermal growth factor receptor mediated signal transduction)

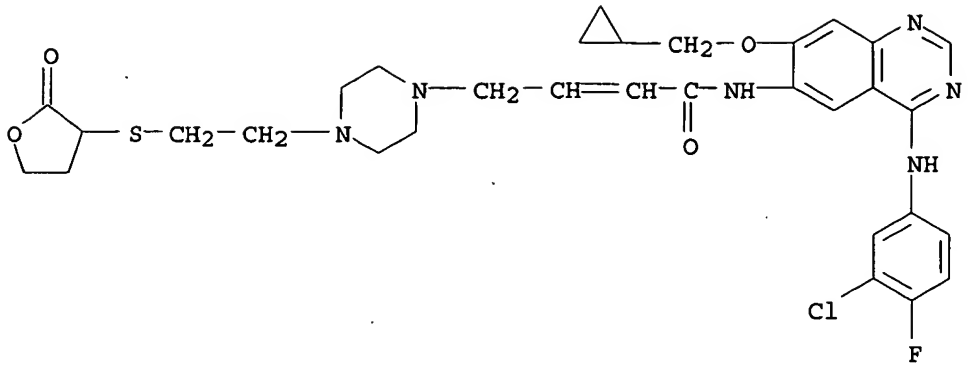
RN 365532-35-0 CAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-[4-(tetrahydro-2-oxo-3-furanyl)-1-piperazinyl]- (9CI) (CA INDEX NAME)



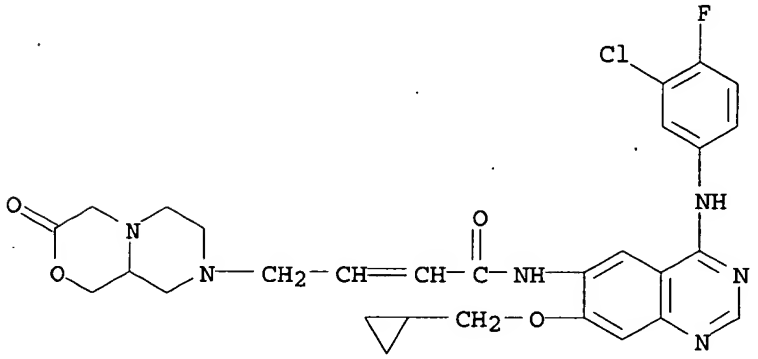
RN 365532-39-4 CAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-[4-(tetrahydro-5-oxo-3-furanyl)-1-piperazinyl]- (9CI) (CA INDEX NAME)



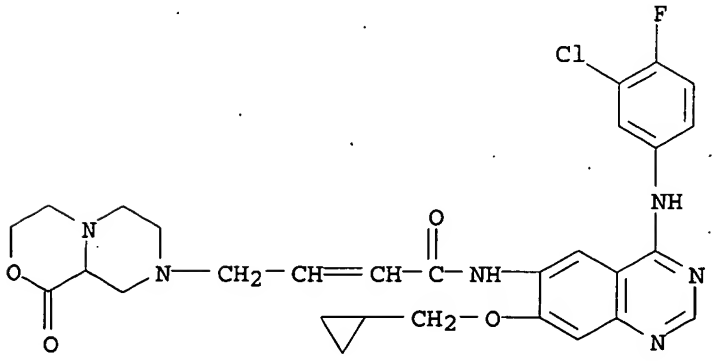
RN 365532-42-9 CAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-[4-[2-[(tetrahydro-2-oxo-3-furanyl)thio]ethyl]-1-piperazinyl]- (9CI) (CA INDEX NAME)



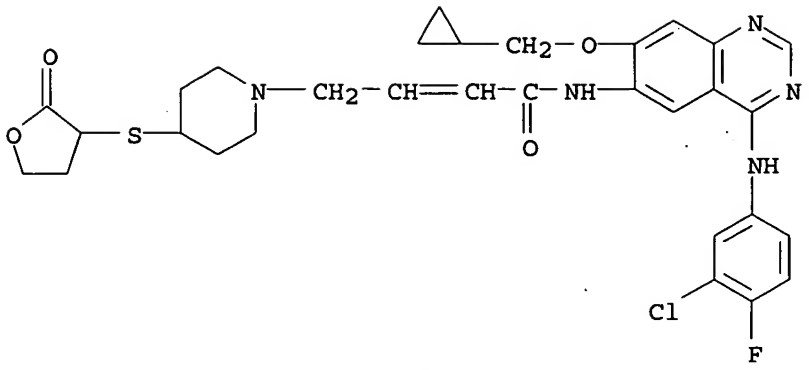
RN 365532-45-2 CAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-(hexahydro-3-oxopyrazino[2,1-c][1,4]oxazin-8(1H)-yl)-(9CI) (CA INDEX NAME)



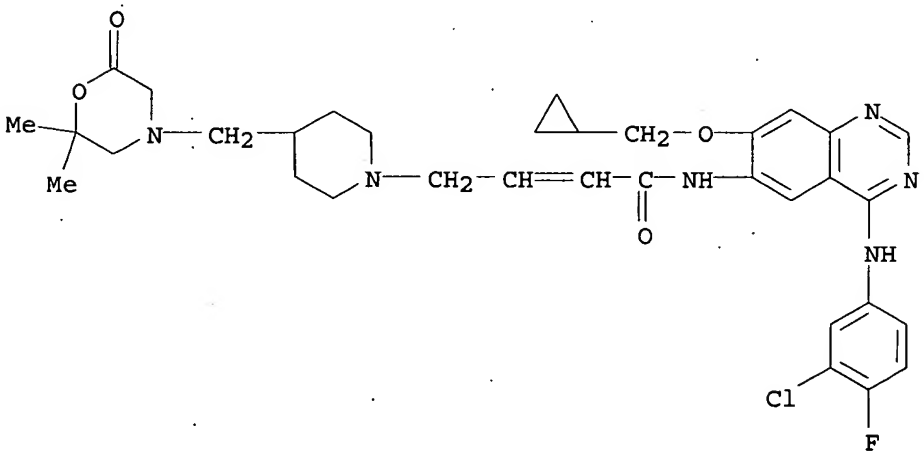
RN 365532-47-4 CAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-(hexahydro-1-oxopyrazino[2,1-c][1,4]oxazin-8(1H)-yl)-(9CI) (CA INDEX NAME)



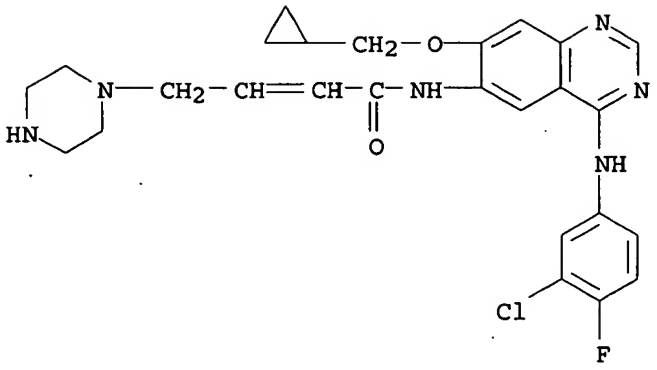
RN 365532-48-5 CAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-[4-[(tetrahydro-2-oxo-3-furanyl)thio]-1-piperidinyl]-(9CI) (CA INDEX NAME)



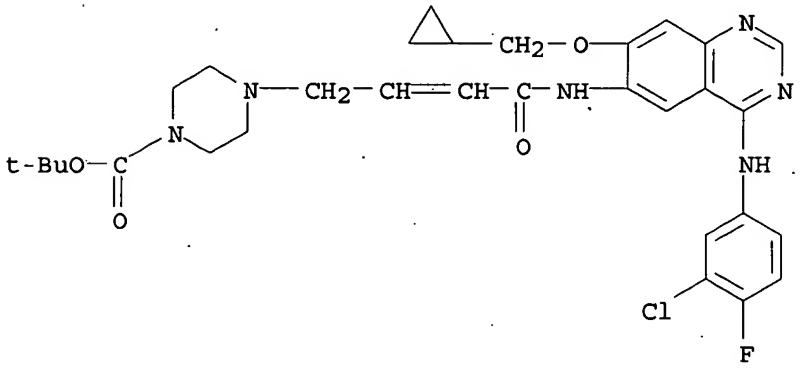
RN 365532-49-6 CAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-[4-[(2,2-dimethyl-6-oxo-4-morpholinyl)methyl]-1-piperidinyl]- (9CI) (CA INDEX NAME)



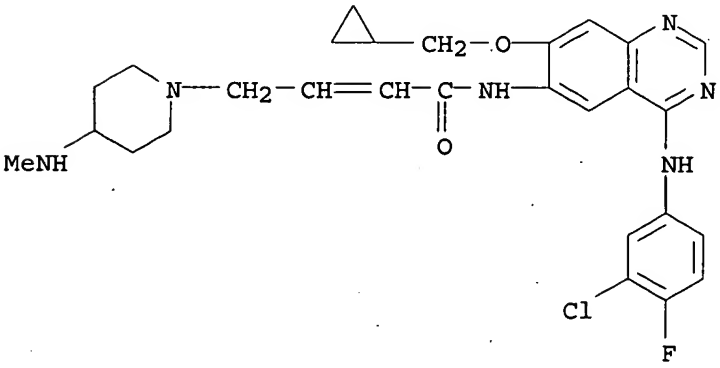
IT **290303-47-8P 290304-01-7P 365532-06-5P**
365532-10-1P 365532-18-9P 365532-21-4P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of bicyclic heterocycles as inhibitors of epidermal growth factor receptor mediated signal transduction)
RN 290303-47-8 CAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-(1-piperazinyl)- (9CI) (CA INDEX NAME)



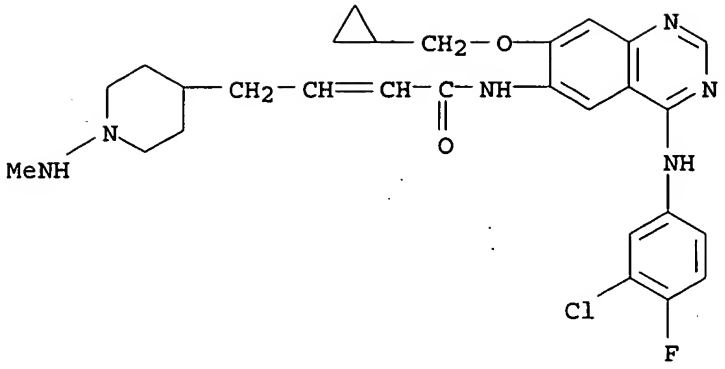
RN 290304-01-7 CAPLUS
CN 1-Piperazinecarboxylic acid, 4-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]amino]-4-oxo-2-butenyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



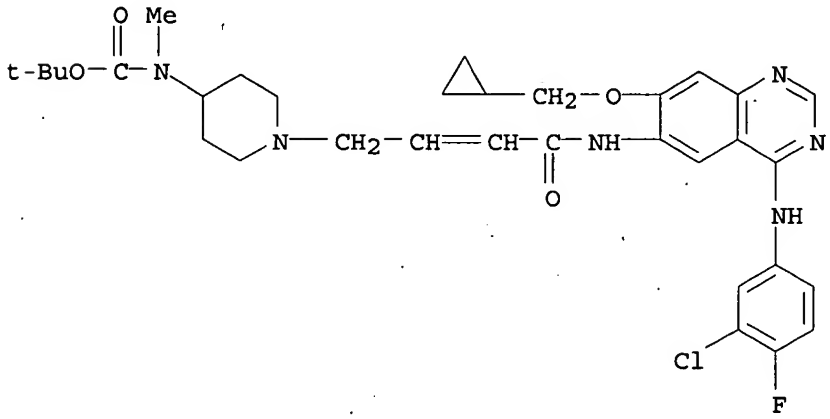
RN 365532-06-5 CAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-[4-(methylamino)-1-piperidinyl]- (9CI) (CA INDEX NAME)



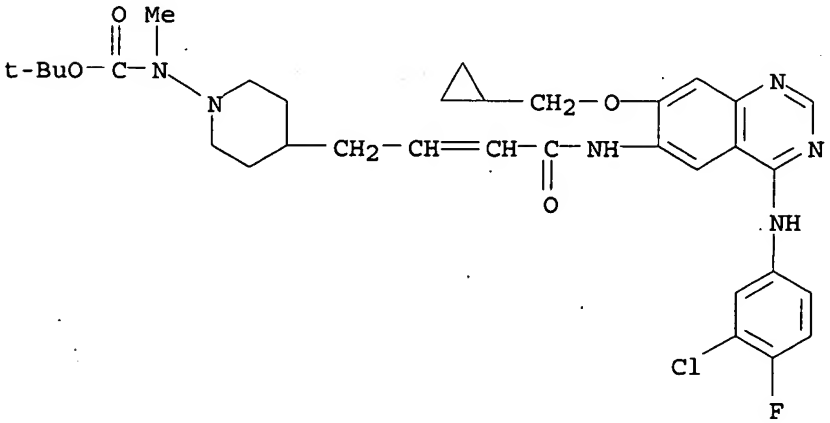
RN 365532-10-1 CAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-[1-(methylamino)-4-piperidinyl]- (9CI) (CA INDEX NAME)



RN 365532-18-9 CAPLUS
CN Carbamic acid, [1-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]amino]-4-oxo-2-butenyl]-4-piperidinyl]methyl-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



RN 365532-21-4 CAPLUS
CN Carbamic acid, [4-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]amino]-4-oxo-2-butenyl]-1-piperidinyl]methyl-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

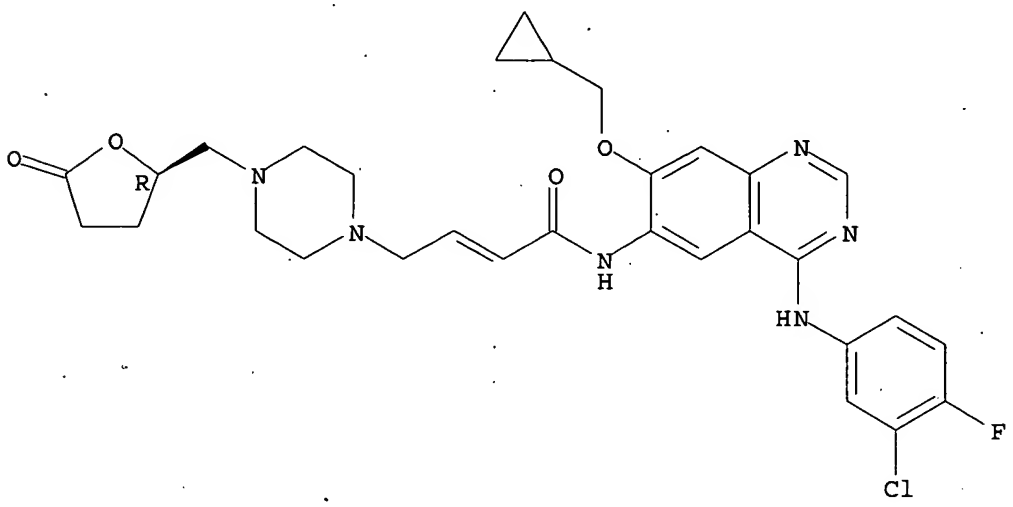


IT **365532-36-1P 365532-37-2P 365532-38-3P**

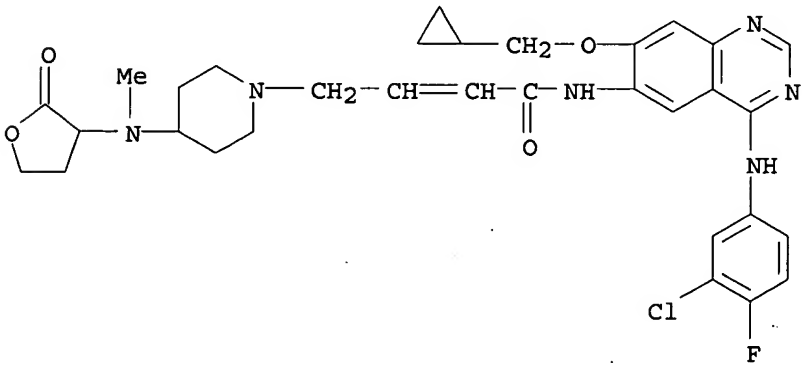
365532-41-8P 365532-43-0P 365532-44-1P
365532-46-3P
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of bicyclic heterocycles as inhibitors of epidermal growth factor receptor mediated signal transduction)

RN 365532-36-1 CAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-[4-[[(2R)-tetrahydro-5-oxo-2-furanyl]methyl]-1-piperazinyl]- (9CI) (CA INDEX NAME)

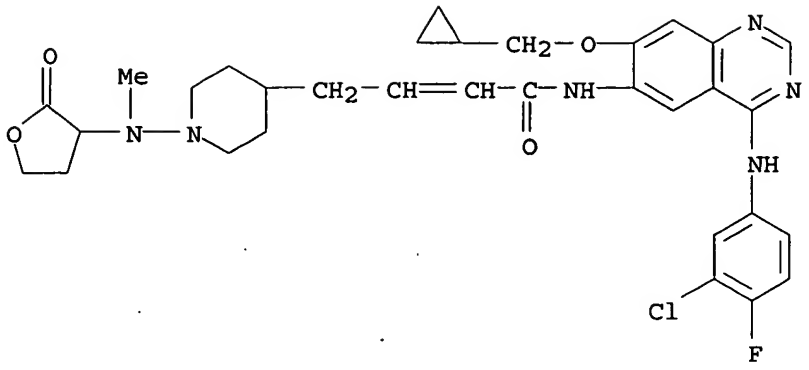
Absolute stereochemistry.
Double bond geometry unknown.



RN 365532-37-2 CAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-[4-[methyl(tetrahydro-2-oxo-3-furanyl)amino]-1-piperidinyl]- (9CI) (CA INDEX NAME)

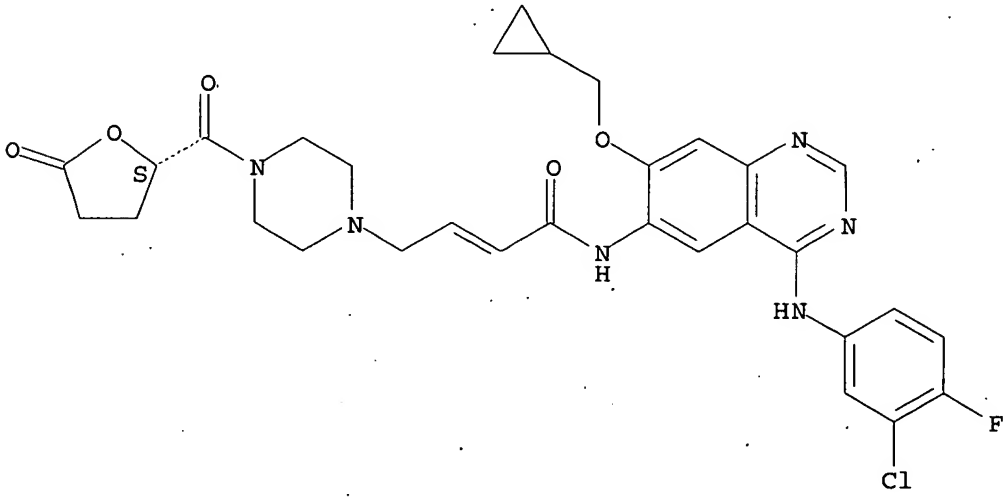


RN 365532-38-3 CAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-[1-[methyl(tetrahydro-2-oxo-3-furanyl)amino]-4-piperidinyl]- (9CI) (CA INDEX NAME)

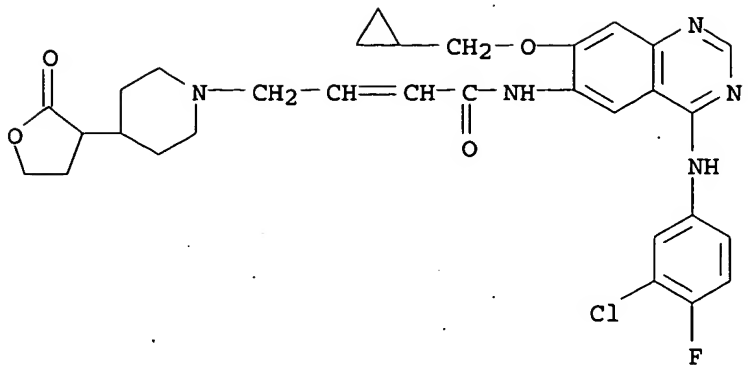


RN 365532-41-8 CAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-[4-[[(2S)-tetrahydro-5-oxo-2-furanyl]carbonyl]-1-piperazinyl]- (9CI) (CA INDEX NAME)

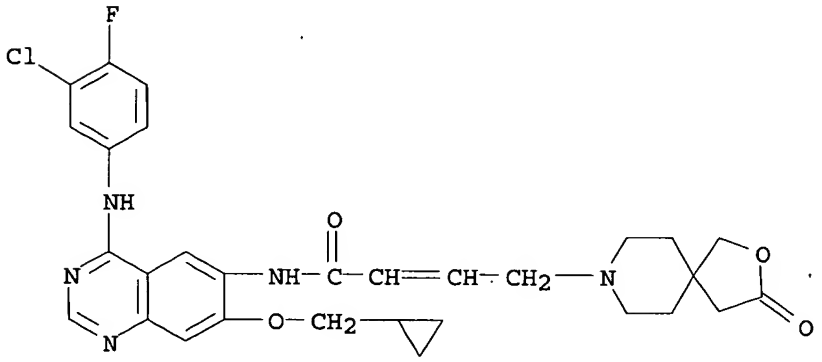
Absolute stereochemistry.
Double bond geometry unknown.



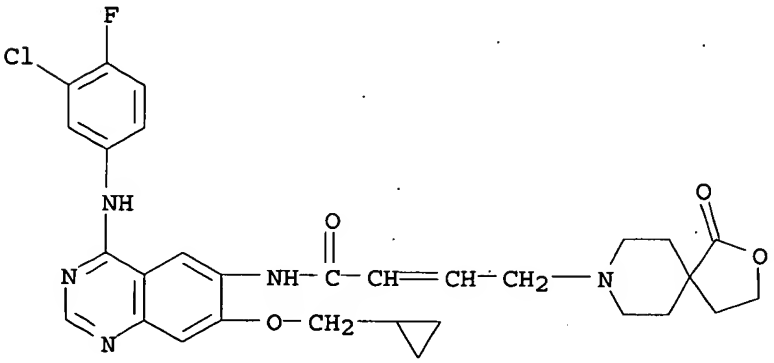
RN 365532-43-0 CAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-[4-(tetrahydro-2-oxo-3-furanyl)-1-piperidinyl]- (9CI) (CA INDEX NAME)



RN 365532-44-1 CAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-(3-oxo-2-oxa-8-azaspiro[4.5]dec-8-yl)- (9CI) (CA INDEX NAME)



RN 365532-46-3 CAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-(1-oxo-2-oxa-8-azaspiro[4.5]dec-8-yl)- (9CI) (CA INDEX NAME)



L3 ANSWER 6 OF 13 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2001:514231 CAPLUS
DOCUMENT NUMBER: 135:251424
TITLE: 6-Substituted-4-(3-bromophenylamino)quinazolines as

10/ 023,099

Putative Irreversible Inhibitors of the Epidermal Growth Factor Receptor (EGFR) and Human Epidermal Growth Factor Receptor (HER-2) Tyrosine Kinases with Enhanced Antitumor Activity

AUTHOR(S): Tsou, Hwei-Ru; Mamuya, Nellie; Johnson, Bernard D.; Reich, Marvin F.; Gruber, Brian C.; Ye, Fei; Nilakantan, Ramaswamy; Shen, Ru; Discafani, Carolyn; DeBlanc, Ronald; Davis, Rachel; Koehn, Frank E.; Greenberger, Lee M.; Wang, Yu-Fen; Wissner, Allan

CORPORATE SOURCE: Wyeth-Ayerst Research A Division of American Home Products, Pearl River, NY, 10965-1215, USA

SOURCE: Journal of Medicinal Chemistry (2001), 44(17), 2719-2734
CODEN: JMCMAR; ISSN: 0022-2623

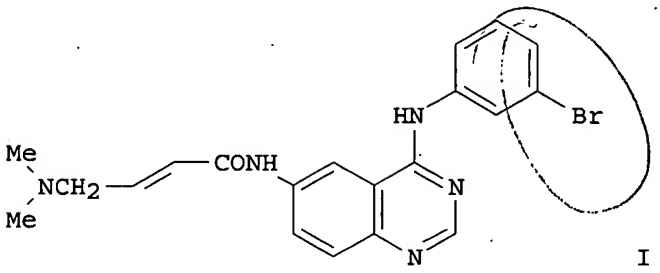
PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 135:251424

GI



I

AB A series of new 6-substituted-4-(3-bromophenylamino)quinazoline derivs. that may function as irreversible inhibitors of epidermal growth factor receptor (EGFR) and human epidermal growth factor receptor (HER-2) tyrosine kinases have been prepd. These inhibitors have, at the C-6 position, butynamide, crotonamide, and methacrylamide Michael acceptors bearing water-solubilizing substituents. These compds. were prepd. by acylation of 6-amino-4-(3-bromophenylamino)quinazoline with unsatd. acid chlorides or mixed anhydrides. We show that attaching a basic functional group onto the Michael acceptor results in greater reactivity, due to intramol. catalysis of the Michael addn. and/or an inductive effect of the protonated basic group. This, along with improved water soly., results in compds. with enhanced biol. properties. We present mol. modeling and exptl. evidence that these inhibitors interact covalently with the target enzymes. One compd., (I) was shown to have excellent oral activity in a human epidermoid carcinoma (A431) xenograft model in nude mice.

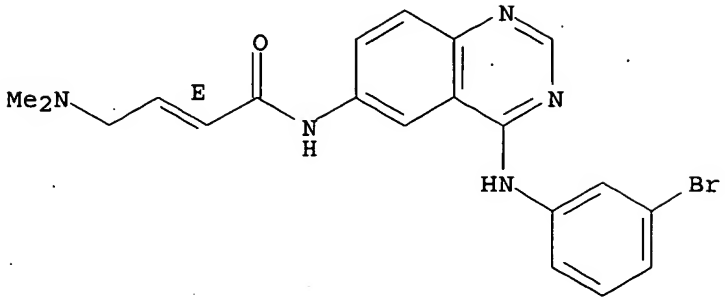
IT **361392-73-6P 361392-74-7P 361392-75-8P 361392-76-9P 361392-77-0P 361392-78-1P 361392-79-2P 361392-80-5P 361392-81-6P 361392-82-7P 361392-83-8P 361392-89-4P 361392-90-7P**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. and structure activity relations of antitumor (bromophenylamino)quinazolines as putative irreversible inhibitors of EGFR and human epidermal growth factor receptor (HER-2) tyrosine kinase)

RN 361392-73-6 CAPLUS

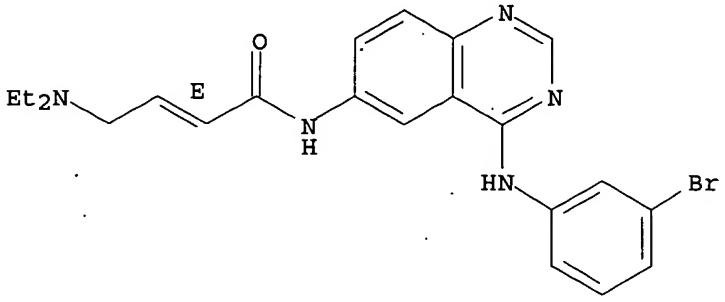
CN 2-Butenamide, N-[4-[(3-bromophenyl)amino]-6-quinazolinyl]-4-(dimethylamino)-, (2E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



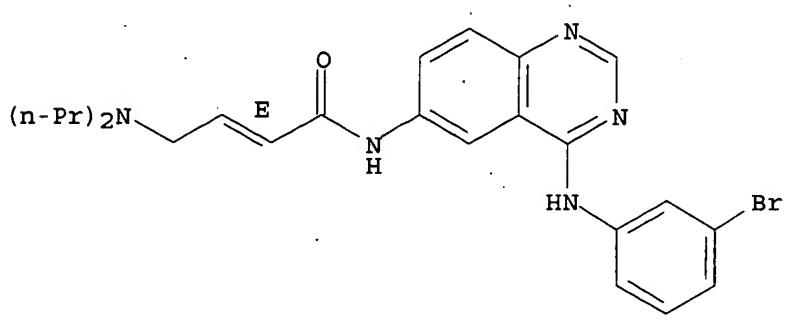
RN 361392-74-7 CAPLUS
CN 2-Butenamide, N-[4-[(3-bromophenyl)amino]-6-quinazolinyl]-4-(diethylamino)-, (2E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



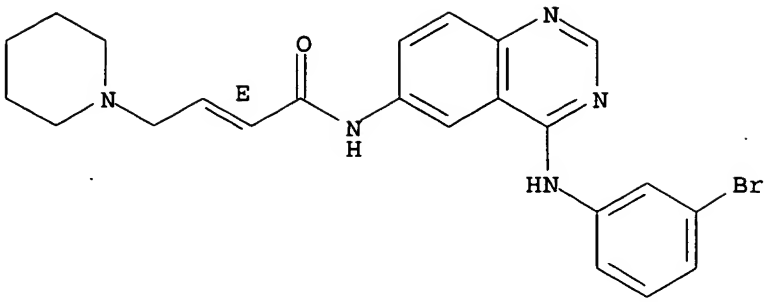
RN 361392-75-8 CAPLUS
CN 2-Butenamide, N-[4-[(3-bromophenyl)amino]-6-quinazolinyl]-4-(dipropylamino)-, (2E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



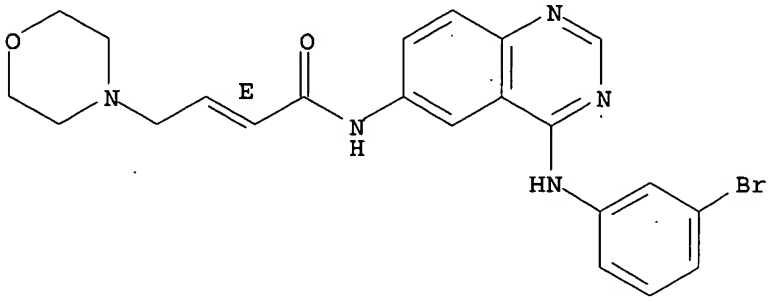
RN 361392-76-9 CAPLUS
CN 2-Butenamide, N-[4-[(3-bromophenyl)amino]-6-quinazolinyl]-4-(1-piperidinyl)-, (2E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



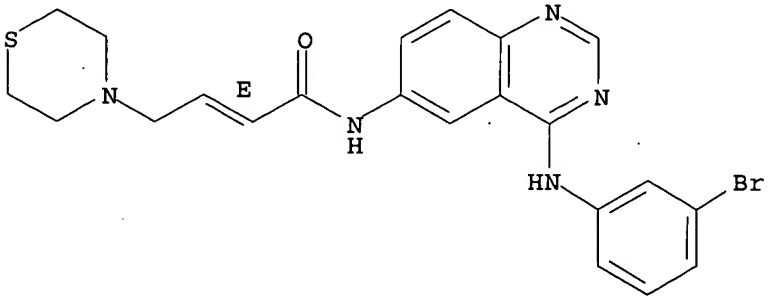
RN 361392-77-0 CAPLUS
CN 2-Butenamide, N-[4-[(3-bromophenyl)amino]-6-quinazolinyl]-4-(4-morpholinyl)-, (2E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



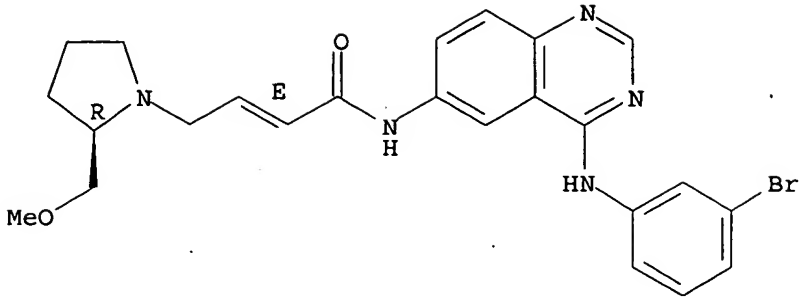
RN 361392-78-1 CAPLUS
CN 2-Butenamide, N-[4-[(3-bromophenyl)amino]-6-quinazolinyl]-4-(4-thiomorpholinyl)-, (2E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



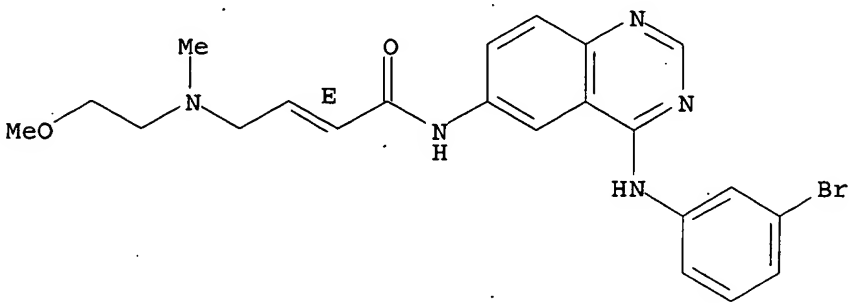
RN 361392-79-2 CAPLUS
CN 2-Butenamide, N-[4-[(3-bromophenyl)amino]-6-quinazolinyl]-4-[(2R)-2-(methoxymethyl)-1-pyrrolidinyl]-, (2E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



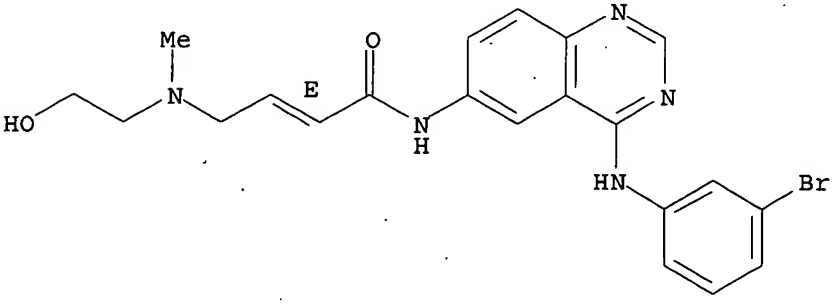
RN 361392-80-5 CAPLUS
CN 2-Butenamide, N-[4-[(3-bromophenyl)amino]-6-quinazolinyl]-4-[(2-methoxyethyl)methylamino]-, (2E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



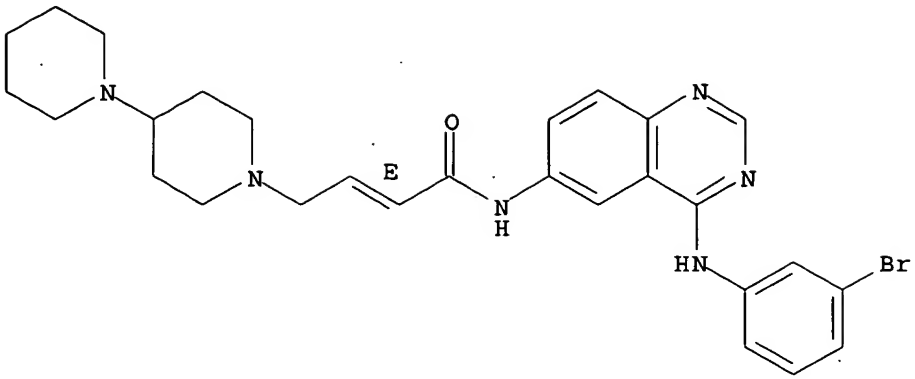
RN 361392-81-6 CAPLUS
CN 2-Butenamide, N-[4-[(3-bromophenyl)amino]-6-quinazolinyl]-4-[(2-hydroxyethyl)methylamino]-, (2E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



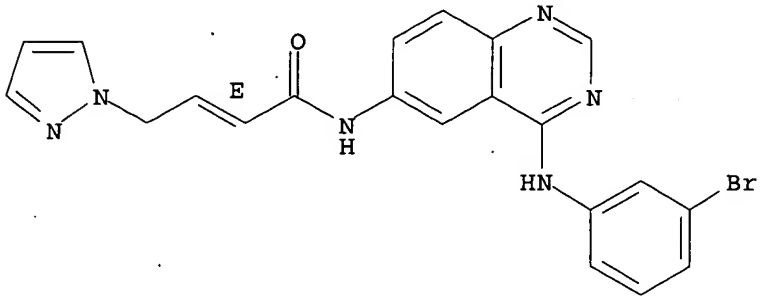
RN 361392-82-7 CAPLUS
CN 2-Butenamide, 4-[1,4'-bipiperidin]-1'-yl-N-[4-[(3-bromophenyl)amino]-6-quinazolinyl]-, (2E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



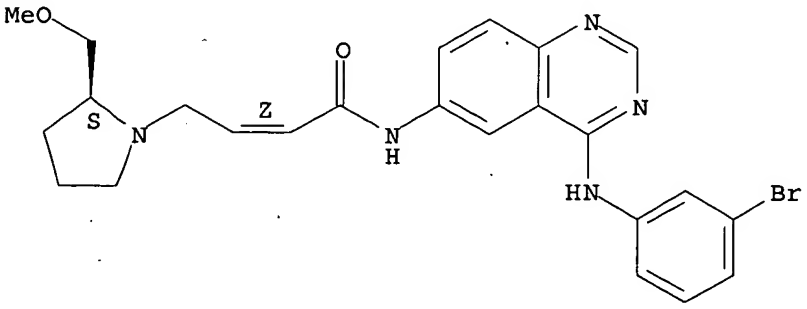
RN 361392-83-8 CAPLUS
CN 2-Butenamide, N-[4-[(3-bromophenyl)amino]-6-quinazolinyl]-4-(1H-pyrazol-1-yl)-, (2E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



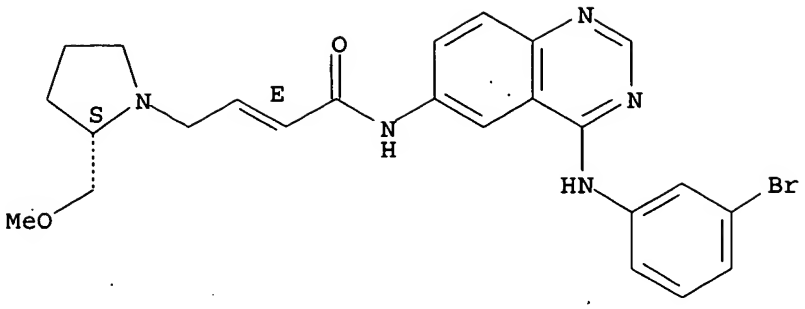
RN 361392-89-4 CAPLUS
CN 2-Butenamide, N-[4-[(3-bromophenyl)amino]-6-quinazolinyl]-4-[(2S)-2-(methoxymethyl)-1-pyrrolidinyl]-, (2Z)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



RN 361392-90-7 CAPLUS
CN 2-Butenamide, N-[4-[(3-bromophenyl)amino]-6-quinazolinyl]-4-[(2S)-2-(methoxymethyl)-1-pyrrolidinyl]-, (2E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



REFERENCE COUNT: 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 7 OF 13 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2001:185 CAPLUS
DOCUMENT NUMBER: 134:207783
TITLE: Tyrosine kinase inhibitors. 18. 6-Substituted 4-anilinoquinazolines and 4-anilinopyrido[3,4-d]pyrimidines as soluble, irreversible inhibitors of the epidermal growth factor receptor
AUTHOR(S): Smaill, Jeff B.; Showalter, H. D. Hollis; Zhou, Hairong; Bridges, Alexander J.; McNamara, Dennis J.; Fry, David W.; Nelson, James M.; Sherwood, Veronika; Vincent, Patrick W.; Roberts, Bill J.; Elliott, William L.; Denny, William A.
CORPORATE SOURCE: Auckland Cancer Society Research Centre Faculty of Medicine and Health Science, The University of Auckland, Auckland, 92019, N. Z.
SOURCE: Journal of Medicinal Chemistry (2001), 44(3), 429-440
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB 4-Anilinoquinazoline- and 4-anilinopyrido[3,4-d]pyrimidine-6-acrylamides are potent pan-erbB tyrosine kinase inactivators, and one example (CI-1033) is in clin. trial. A series of analogs with a variety of Michael acceptor units at the 6-position, I [X = N, C, R1 = H, Me, (CH2)2NMe2, etc., R2 = H, Me, R3 = H, cis-Cl, CF3, etc.], II, and III (X = N, C, R1 = NHSO2CH:CH2, SO2CH2CH2OH, SO2CH:CH2, SOCH:CH2), were prepd. to define the structural requirements for irreversible inhibition. A particular goal was to det. whether addnl. functions to increase soly. could be appended to the Michael acceptor. Substituted acrylamides were prepd. by direct acylation of the corresponding 6-amines with the requisite acid or acid chloride. Vinylsulfonamide derivs. were obtained by acylation of the amines with chloroethylsulfonyl chloride followed by base-promoted elimination. Vinylsulfone and vinylsulfine derivs. were prepd. by oxidn. and base elimination of a hydroxyethylthio intermediate. The compds. were evaluated for their inhibition of phosphorylation of the isolated EGFR enzyme and for inhibition of EGF-stimulated autophosphorylation of EGFR in A431 cells and of heregulin-stimulated autophosphorylation of erbB2 in MDA-MB 453 cells. Substitution at the nitrogen of the acrylamide was tolerated only with a Me group; larger

substituents were dystherapeutic, and no substitution at all was tolerated at the acrylamide .alpha.-carbon. In contrast, while electron-donating groups at the acrylamide .beta.-carbon were not useful, even quite large electron-withdrawing groups (which increase its electrophilicity) were tolerated. A series of derivs. with soly.-enhancing substituents linked to the acrylamide .beta.-carbon via amides were potent irreversible inhibitors of isolated EGFR (IC50s = 0.4-1.1 nM), with weakly basic morpholine and imidazole derivs. being the best. Vinylsulfonamides were also potent and irreversible inhibitors, but vinylsulfones and vinylsulfines were reversible and only poorly active. Two compds. were evaluated against A431, H125, and MCF-7 xenografts in nude mice but were inferior in these assays to the clin. trial compd. CI-1033.

IT **198960-34-8P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(prepn., epidermal growth factor receptor inhibitory activity, and structure-activity relationship of anilinoquinazolines and -pyridopyrimidines)

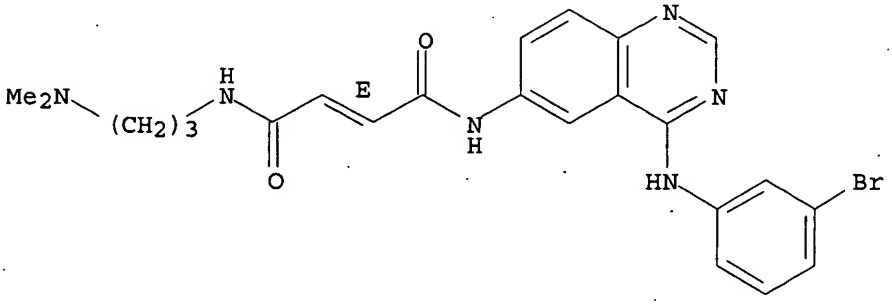
RN 198960-34-8 CAPLUS

CN 2-Butenediamide, N-[4-[(3-bromophenyl)amino]-6-quinazolinyl]-N'-[3-(dimethylamino)propyl]-, (2E)-, tris(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

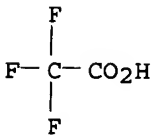
CRN 198960-33-7
CMF C23 H25 Br N6 O2

Double bond geometry as shown.



CM 2

CRN 76-05-1
CMF C2 H F3 O2



REFERENCE COUNT: 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 8 OF 13 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2000:911231 CAPLUS

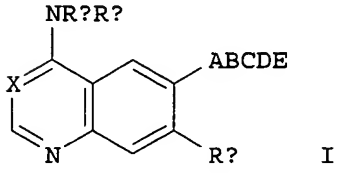
10/ 023,099

DOCUMENT NUMBER: 134:71599
TITLE: Preparation of aminoquinazolines and aminoquinolines as epidermal growth factor receptor signal transduction inhibitors.
INVENTOR(S): Himmelsbach, Frank; Langkopf, Elke; Metz, Thomas; Solca, Flavio; Jung, Birgit; Baum, Anke
PATENT ASSIGNEE(S): Boehringer Ingelheim Pharma K.-G., Germany
SOURCE: PCT Int. Appl., 104 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000078735	A1	20001228	WO 2000-EP5547	20000616
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
DE 19928281	A1	20001228	DE 1999-19928281	19990621
DE 10023085	A1	20011115	DE 2000-10023085	20000511
BR 2000011834	A	20020312	BR 2000-11834	20000616
EP 1194418	A1	20020410	EP 2000-936888	20000616
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2003502410	T2	20030121	JP 2001-504901	20000616
EE 200100695	A	20030217	EE 2001-695	20000616
BG 106189	A	20020830	BG 2001-106189	20011207
US 2002169180	A1	20021114	US 2001-16280	20011210
NO 2001006185	A	20011218	NO 2001-6185	20011218

PRIORITY APPLN. INFO::
DE 1999-19928281 A 19990621
US 1999-146644P P 19990730
DE 2000-10023085 A 20000511
WO 2000-EP5547 W 20000616

OTHER SOURCE(S): MARPAT 134:71599
GI



I

AB Title compds. [I; Ra = H, alkyl; Rb = (substituted) Ph, PhCH2, PhCH2CH2; Rc = (substituted) cycloalkoxy, cycloalkylalkoxy; A = (alkyl-substituted) imino; B = CO, SO2; C = (substituted) allenylene, vinylene, butadienylene, ethynylene; D = (fluorinated) alkylene, carbonylalkylene, sulfonylalkylene, carbonyloxyalkylene, carbonyliminoalkylene, bond, etc.; E = amino, (substituted) alkylamino, dialkylamino, etc.], were prepd. Thus, 6-amino-4-[(3-bromophenyl)amino]-7-[3-(1-methylpiperidin-4-yl)propoxy]quinazoline (prepn. given) in CH2Cl2 contg. Et3N at -10.degree. was treated with acryloyl chloride in THF to give 35% 4-[(3-

bromophenyl)amino]-7-[3-(1-methylpiperidin-4-yl)propyloxy]-6-[(vinylcarbonyl)amino]quinazoline. The latter inhibited EGF-dependent proliferation of F/L HERC cells with IC50 = <0.35 nM.

IT **314771-10-3P 314771-12-5P 314771-31-8P**
314771-32-9P 314771-33-0P 314771-34-1P
314771-35-2P 314771-36-3P 314771-37-4P
314771-38-5P 314771-45-4P 314771-46-5P
314771-47-6P 314771-48-7P 314771-49-8P
314771-50-1P 314771-51-2P 314771-52-3P
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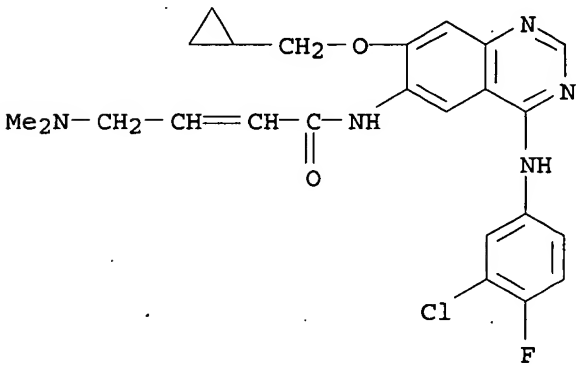
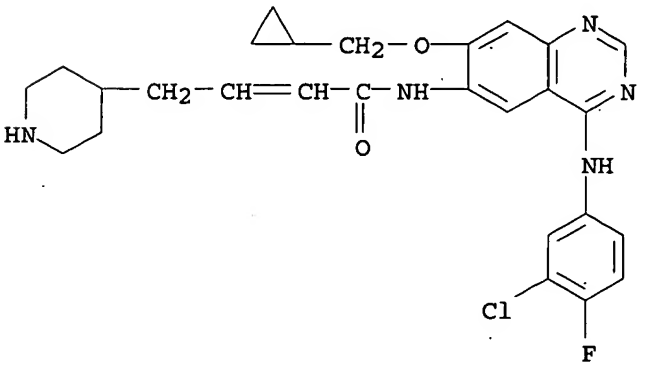
314771-56-7P 314771-57-8P 314771-58-9P
314771-59-0P 314771-60-3P 314771-61-4P
314771-62-5P 314771-63-6P 314771-64-7P
314771-65-8P 314771-66-9P 314771-67-0P
314771-68-1P 314771-69-2P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of aminoquinazolines and aminoquinolines as epidermal growth factor receptor signal transduction inhibitors)

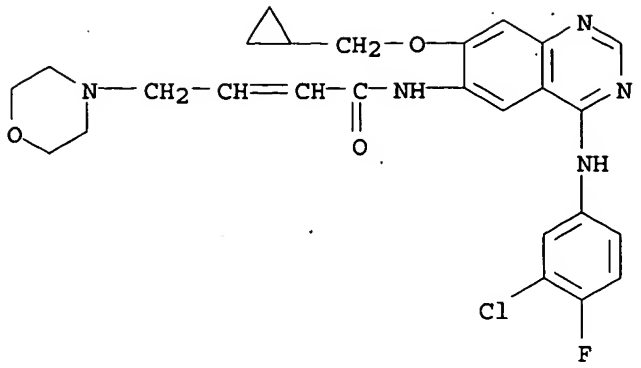
RN 314771-10-3 CAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-(dimethylamino)- (9CI) (CA INDEX NAME)



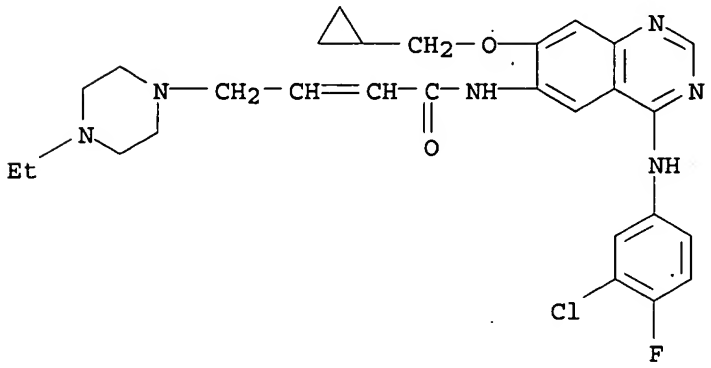
RN 314771-12-5 CAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-(4-piperidinyl)- (9CI) (CA INDEX NAME)



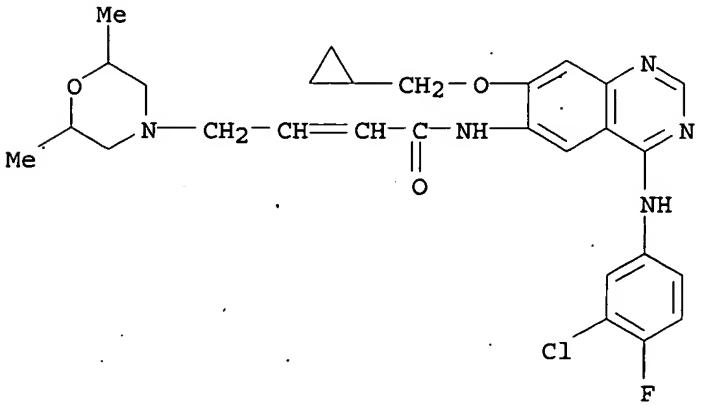
RN 314771-31-8 CAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-(4-morpholinyl)- (9CI) (CA INDEX NAME)



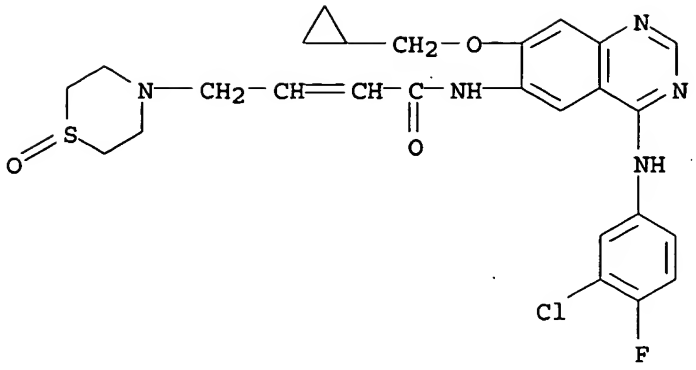
RN 314771-32-9 CAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-(4-ethyl-1-piperazinyl)- (9CI) (CA INDEX NAME)



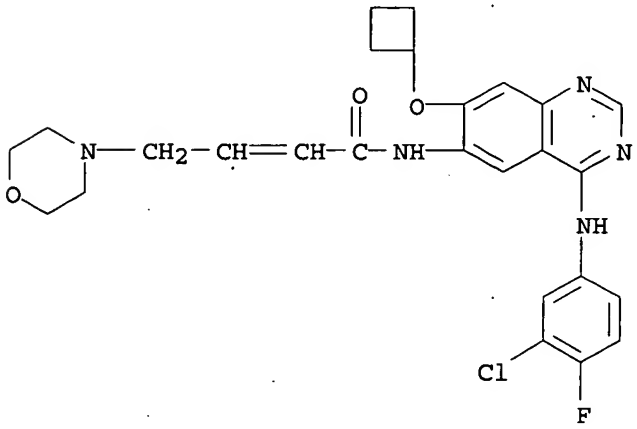
RN 314771-33-0 CAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-(2,6-dimethyl-4-morpholinyl)- (9CI) (CA INDEX NAME)



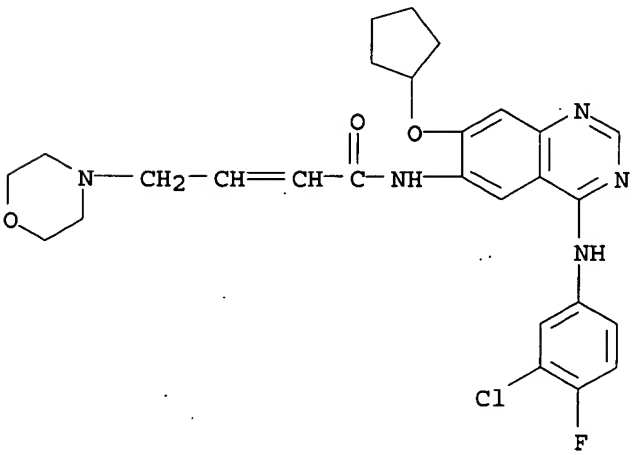
RN 314771-34-1 CAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-(1-oxido-4-thiomorpholinyl)- (9CI) (CA INDEX NAME)



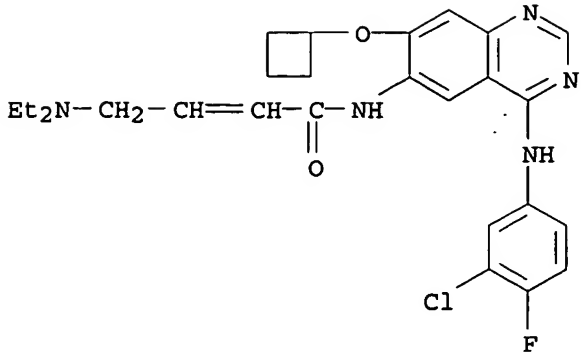
RN 314771-35-2 CAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclobutyloxy)-6-quinazolinyl]-4-(4-morpholinyl)- (9CI) (CA INDEX NAME)



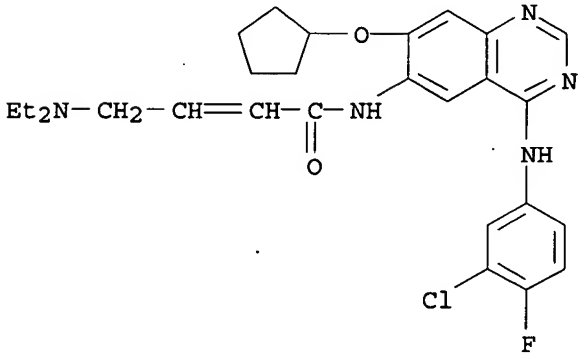
RN 314771-36-3 CAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopentyloxy)-6-quinazolinyl]-4-(4-morpholinyl)- (9CI) (CA INDEX NAME)



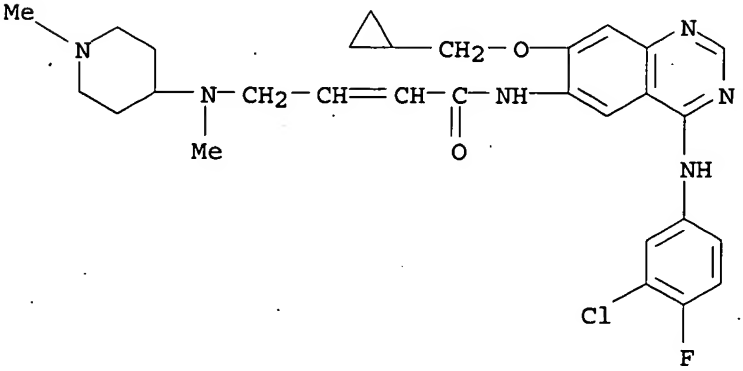
RN 314771-37-4 CAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclobutyloxy)-6-quinazolinyl]-4-(diethylamino)- (9CI) (CA INDEX NAME)



RN 314771-38-5 CAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopentyloxy)-6-quinazolinyl]-4-(diethylamino)- (9CI) (CA INDEX NAME)



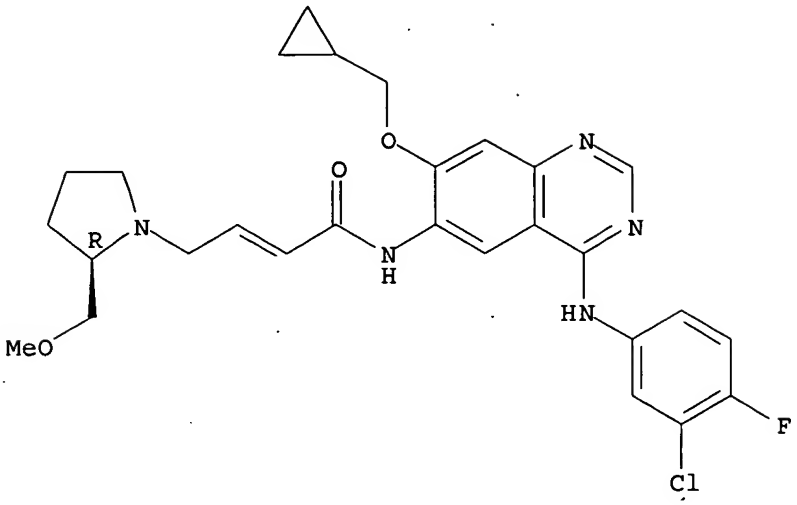
RN 314771-45-4 CAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-[methyl(1-methyl-4-piperidinyl)amino]- (9CI) (CA INDEX NAME)



RN 314771-46-5 CAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-[(2R)-2-(methoxymethyl)-1-pyrrolidinyl]- (9CI) (CA INDEX NAME)

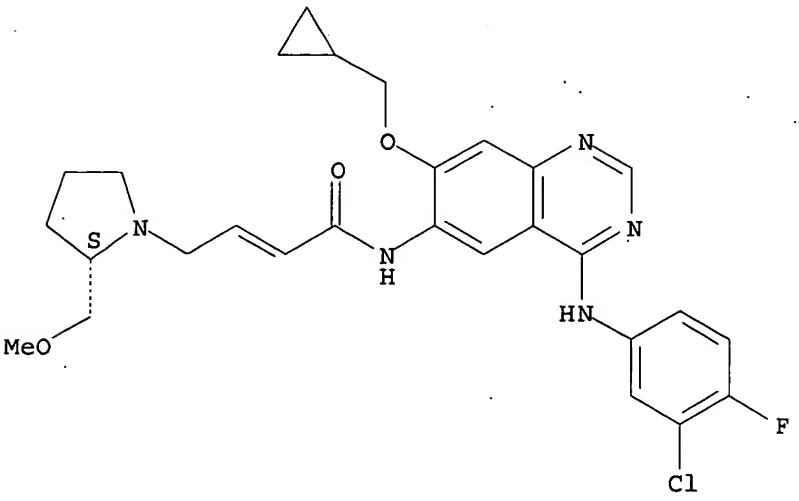
10/ 023,099

Absolute stereochemistry.
Double bond geometry unknown.

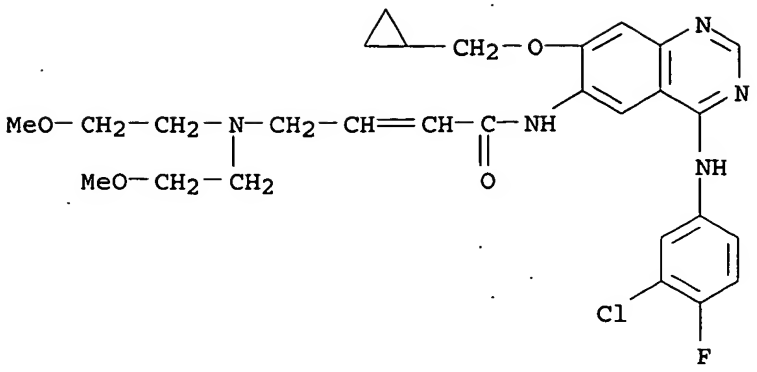


RN 314771-47-6 CAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-[(2S)-2-(methoxymethyl)-1-pyrrolidinyl]- (9CI) (CA INDEX NAME)

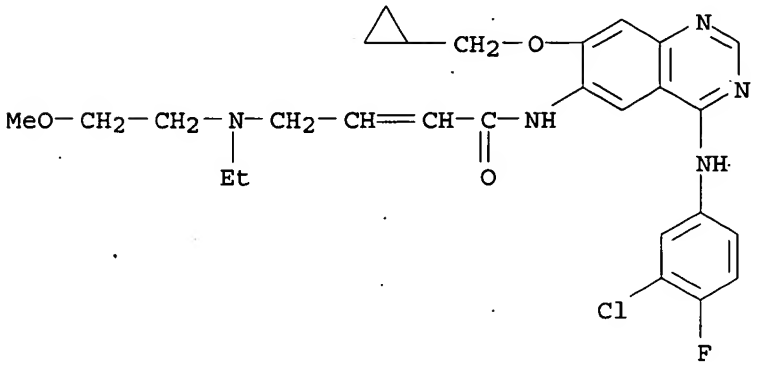
Absolute stereochemistry.
Double bond geometry unknown.



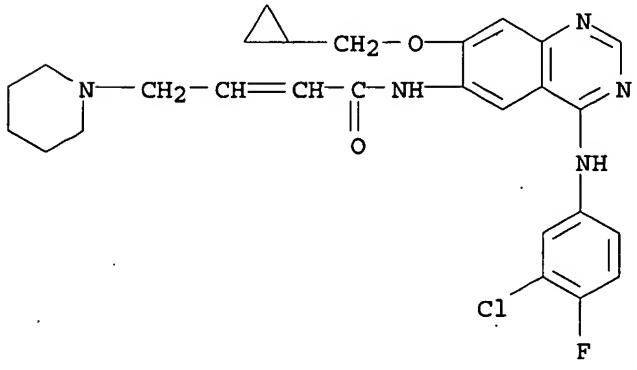
RN 314771-48-7 CAPLUS
CN 2-Butenamide, 4-[bis(2-methoxyethyl)amino]-N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]- (9CI) (CA INDEX NAME)



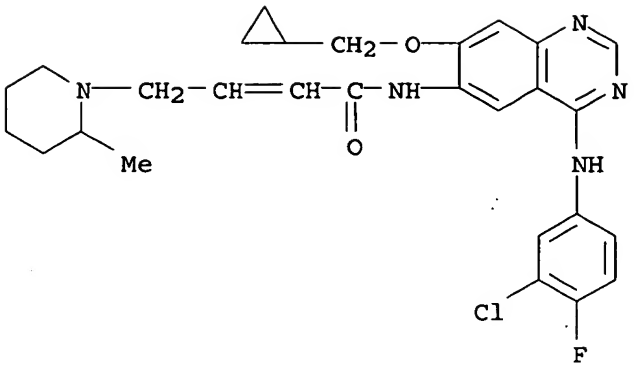
RN 314771-49-8 CAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-[ethyl(2-methoxyethyl)amino]- (9CI) (CA INDEX NAME)



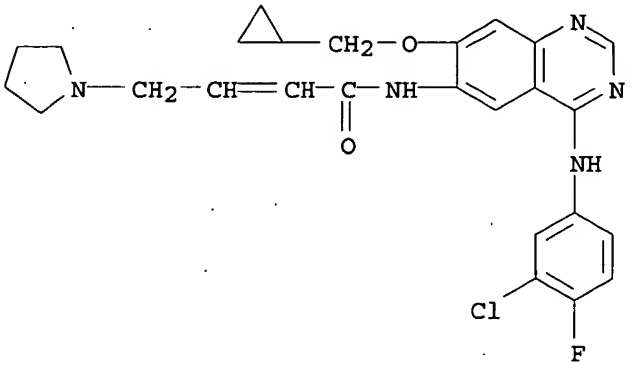
RN 314771-50-1 CAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-(1-piperidinyl)- (9CI) (CA INDEX NAME)



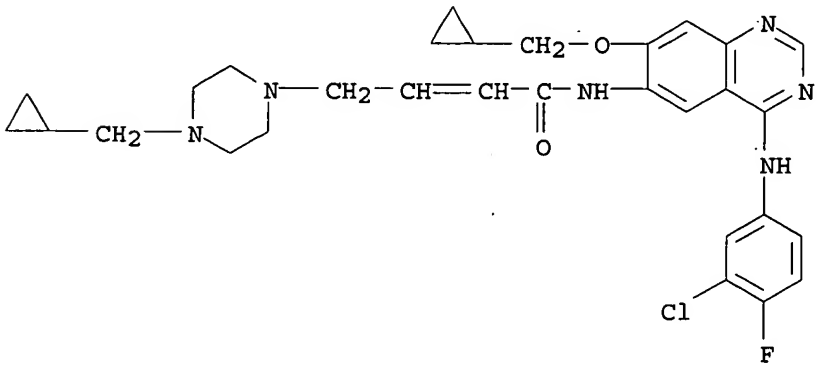
RN 314771-51-2 CAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-(2-methyl-1-piperidinyl)- (9CI) (CA INDEX NAME)



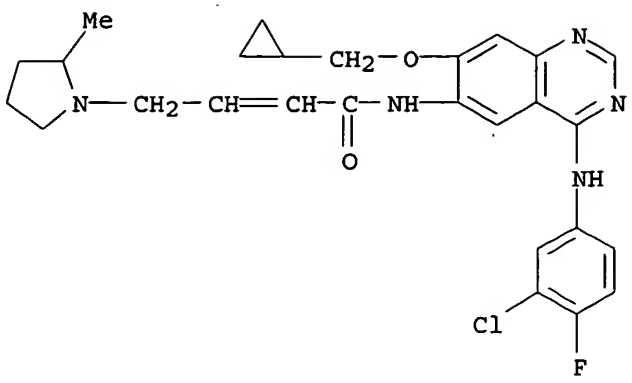
RN 314771-52-3 CAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-(1-pyrrolidinyl)- (9CI) (CA INDEX NAME)



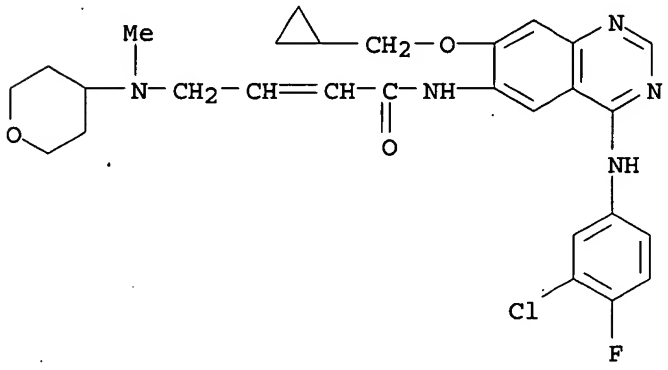
RN 314771-53-4 CAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-[4-(cyclopropylmethyl)-1-piperazinyl]- (9CI) (CA INDEX NAME)



RN 314771-54-5 CAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-(2-methyl-1-pyrrolidinyl)- (9CI) (CA INDEX NAME)

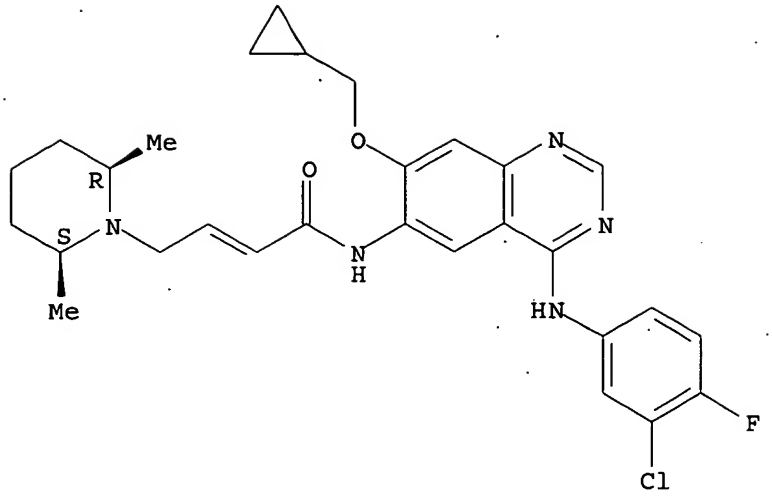


RN 314771-55-6 CAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-[methyl(tetrahydro-2H-pyran-4-yl)amino]- (9CI) (CA INDEX NAME)

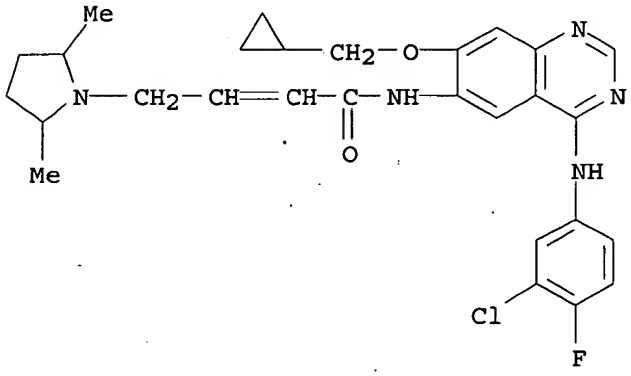


RN 314771-56-7 CAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-[(2R,6S)-2,6-dimethyl-1-piperidinyl]-, rel- (9CI) (CA INDEX NAME)

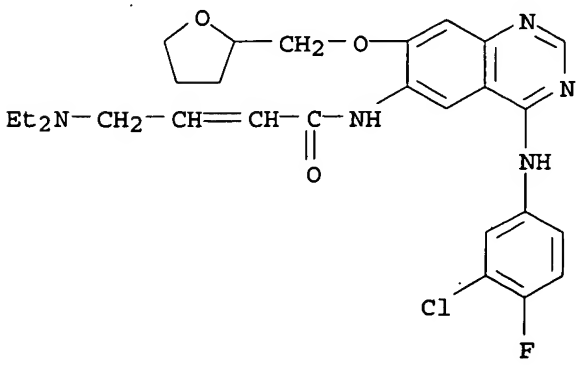
Relative stereochemistry.
Double bond geometry unknown.



RN 314771-57-8 CAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-(2,5-dimethyl-1-pyrrolidinyl)- (9CI) (CA INDEX NAME)



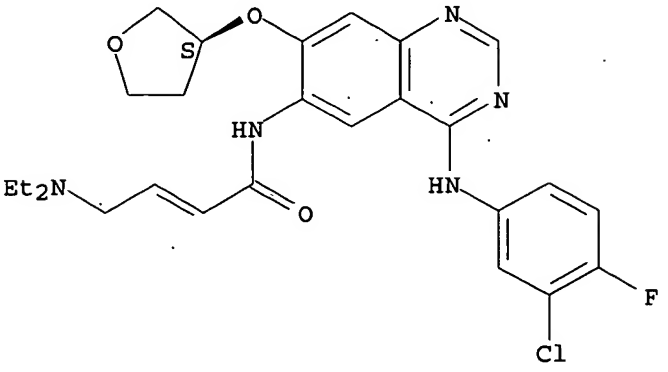
RN 314771-58-9 CAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-[(tetrahydro-2-furanyl)methoxy]-6-quinazolinyl]-4-(diethylamino)- (9CI) (CA INDEX NAME)



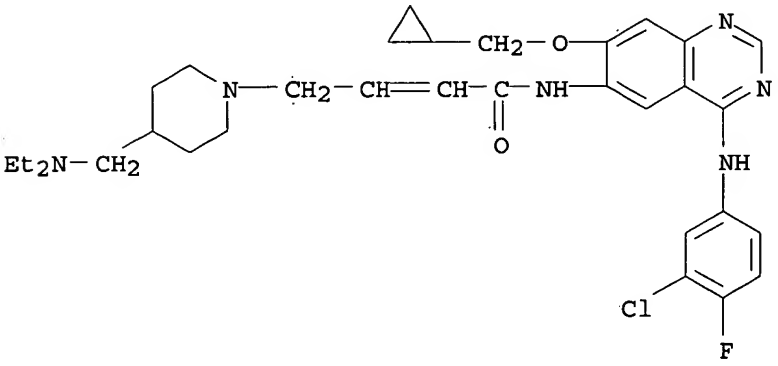
RN 314771-59-0 CAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-[[(3S)-tetrahydro-3-

furanyl]oxy]-6-quinazolinyl]-4-(diethylamino)- (9CI) (CA INDEX NAME)

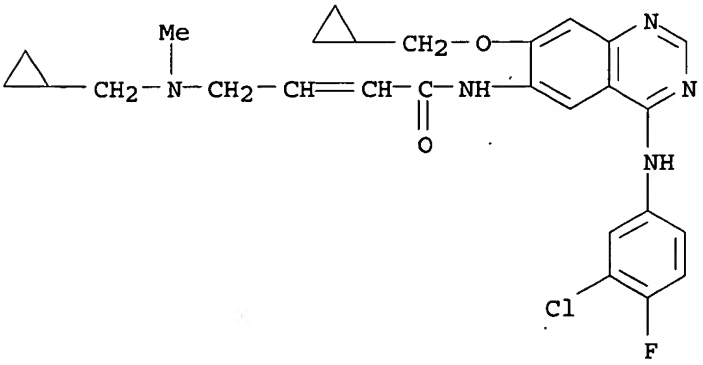
Absolute stereochemistry.
Double bond geometry unknown.



RN 314771-60-3 CAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-[4-[(diethylamino)methyl]-1-piperidinyl]- (9CI) (CA INDEX NAME)

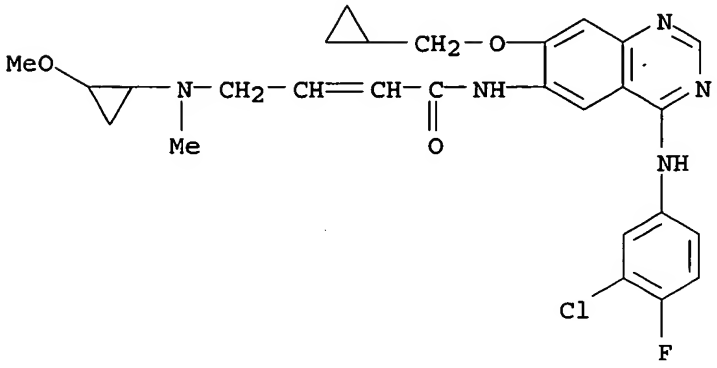


RN 314771-61-4 CAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-[(cyclopropylmethyl)methylamino]- (9CI) (CA INDEX NAME)

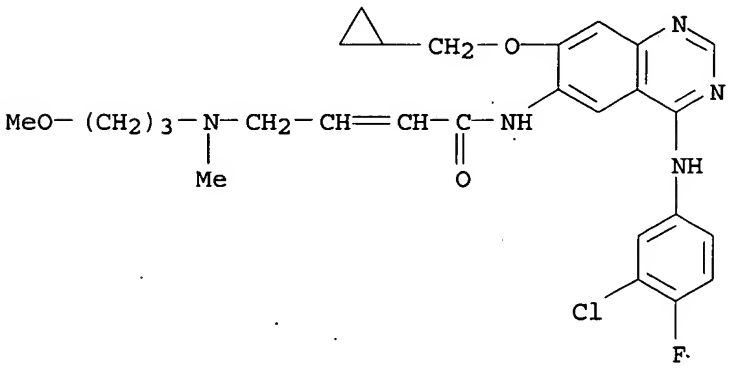


RN 314771-62-5 CAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-

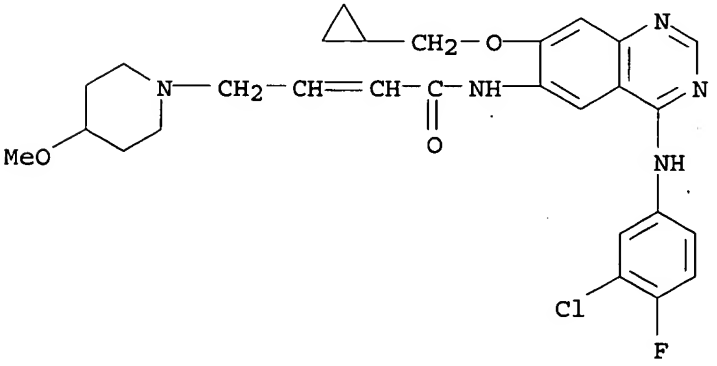
6-quinazolinyl]-4-[(2-methoxycyclopropyl)methylamino]- (9CI) (CA INDEX NAME)



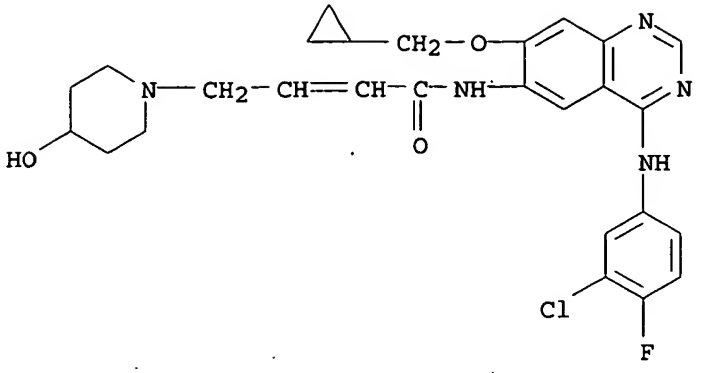
RN 314771-63-6 CAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-[(3-methoxypropyl)methylamino]- (9CI) (CA INDEX NAME)



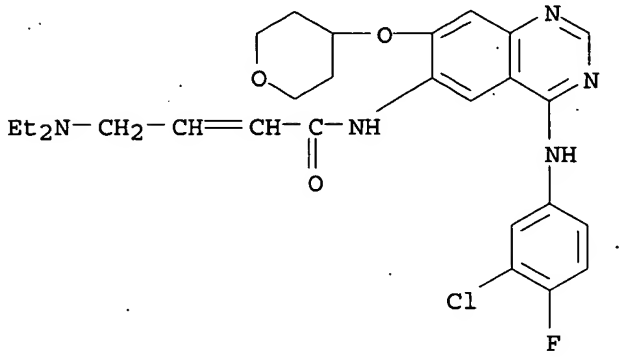
RN 314771-64-7 CAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-(4-methoxy-1-piperidinyl)- (9CI) (CA INDEX NAME)



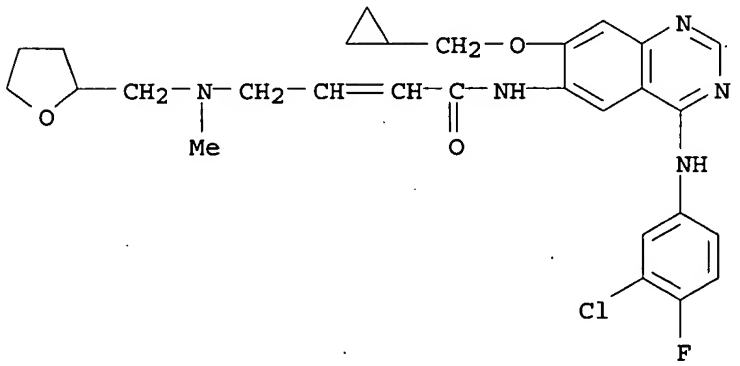
RN 314771-65-8 CAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-(4-hydroxy-1-piperidinyl)- (9CI) (CA INDEX NAME)



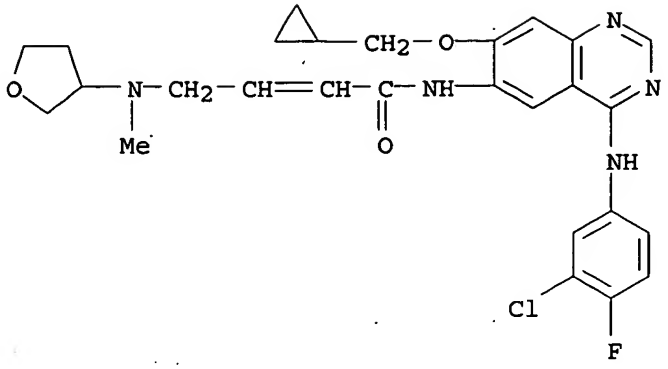
RN 314771-66-9 CAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-[(tetrahydro-2H-pyran-4-yl)oxy]-6-quinazolinyl]-4-(diethylamino)- (9CI) (CA INDEX NAME)



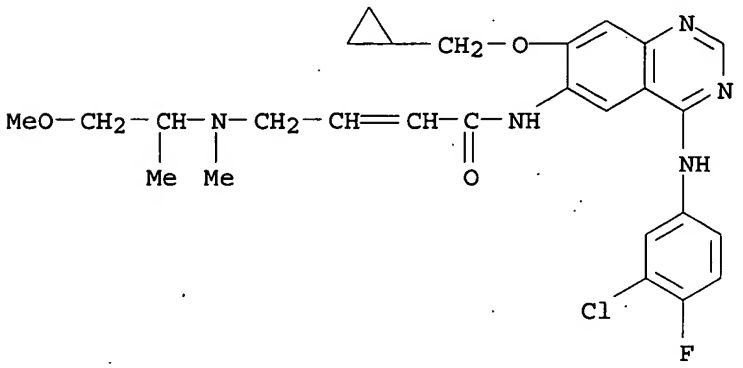
RN 314771-67-0 CAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-[methyl[(tetrahydro-2-furanyl)methyl]amino]- (9CI) (CA INDEX NAME)



RN 314771-68-1 CAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-[methyl(tetrahydro-3-furanyl)amino]- (9CI) (CA INDEX NAME)



RN 314771-69-2 CAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-[(2-methoxy-1-methylethyl)methylamino]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 9 OF 13 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2000:628125 CAPLUS
DOCUMENT NUMBER: 133:207919
TITLE: Preparation of 4-amino-quinazoline and quinoline derivatives having an inhibitory effect on signal transduction mediated by tyrosine kinases useful for treating tumoral diseases, lung and respiratory tract diseases
INVENTOR(S): Himmelsbach, Frank; Langkopf, Elke; Jung, Birgit; Metz, Thomas; Solca, Flavio; Blech, Stefan
PATENT ASSIGNEE(S): Boehringer Ingelheim Pharma K.-G., Germany
SOURCE: PCT Int. Appl., 232 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000051991	A1	20000908	WO 2000-EP1496	20000224

W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA,

MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI,
SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM,
AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE,
DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF,
CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

DE 19908567	A1	20000831	DE 1999-19908567	19990227
DE 19911366	A1	20000921	DE 1999-19911366	19990315
DE 19928306	A1	20001228	DE 1999-19928306	19990621
DE 19954816	A1	20010517	DE 1999-19954816	19991113
CA 2361174	AA	20000908	CA 2000-2361174	20000224
EP 1157011	A1	20011128	EP 2000-910695	20000224
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
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JP 2002538145	T2	20021112	JP 2000-602218	20000224
EE 200100449	A	20021216	EE 2001-449	20000224
BG 105765	A	20020329	BG 2001-105765	20010801
HR 20010617	A1	20021031	HR 2001-617	20010823
NO 2001004114	A	20011015	NO 2001-4114	20010824

PRIORITY APPLN. INFO.:
DE 1999-19908567 A 19990227
DE 1999-19911366 A 19990315
DE 1999-19928306 A 19990621
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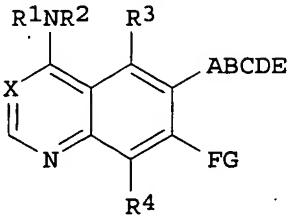
DE 1999-19954816 A 19991113
WO 2000-EP1496 W 20000224

OTHER SOURCE(S): MARPAT 133:207919

GI



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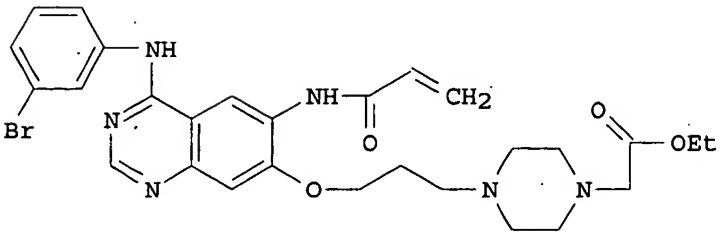


II

AB Title compds. [I; R1 = H, C1-C4-alkyl; R2 = (un)substituted Ph, benzyl, 1-phenylethyl; R3, R4 independently = H, F, Cl, CH3O, CH3OCH2, (CH3)2NCH2, (CH3CH2)2NCH2, pyrrolidino, piperidino, morpholino; X = C(CN), N; A = O, NH, (C1-C4)-alkylN; B = CO, SO2; C = 1,3-allenylene, 1,1-vinylene, 1,2-vinylene, 1,3-butadien-1,4-ylene, with CH3, CF3 substitution; D =

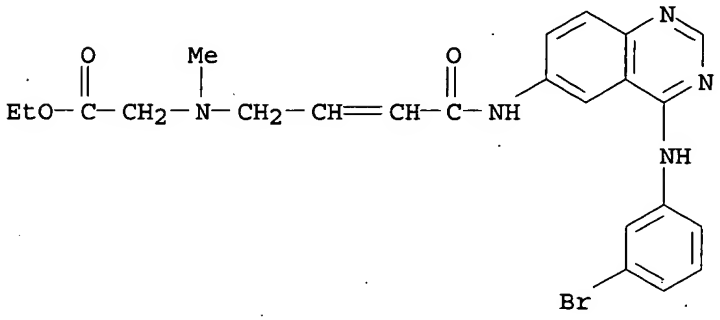
alkylene, CO-alkylene, SO2-alkylene; CO, SO2; E = HOCO(CH2)nNR5, (HO)2P(:O)(CH2)nNR5; n = 1-6; R5 = H, alkyl], tautomers, stereoisomers, and physiol. acceptable salts are prepd. and having valuable pharmacol. properties, particularly an inhibiting effect on signal transduction mediated by tyrosine kinases. Title compds. are useful for treating tumoral diseases, diseases of the lungs and respiratory tract. Thus, the title compd. II was prepd. and tested by Cell Titer 96TM Aq. Nonradioactive Cell Proliferation Assay.

IT **289700-68-1P 290301-75-6P 290301-88-1P 290301-94-9P 290301-96-1P 290302-11-3P 290302-19-1P 290302-25-9P 290302-33-9P 290302-39-5P 290302-47-5P 290302-98-6P 290303-04-7P**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of aminoquinazoline and aminoquinoline derivs. having an inhibitory effect on signal transduction mediated by tyrosine kinases useful for treating tumoral diseases, lung and respiratory tract diseases)

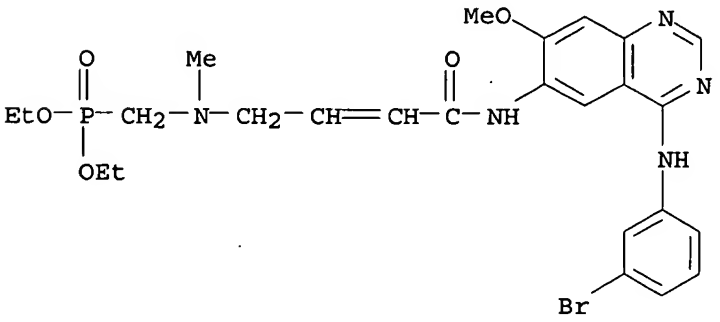
RN 289700-68-1 CAPLUS

CN Glycine, N-[4-[[4-[(3-bromophenyl)amino]-6-quinazolinyl]amino]-4-oxo-2-butenyl]-N-methyl-, ethyl ester (9CI) (CA INDEX NAME)



RN 290301-75-6 CAPLUS

CN Phosphonic acid, [[[4-[[4-[(3-bromophenyl)amino]-7-methoxy-6-quinazolinyl]amino]-4-oxo-2-butenyl]methylamino]methyl]-, diethyl ester (9CI) (CA INDEX NAME)

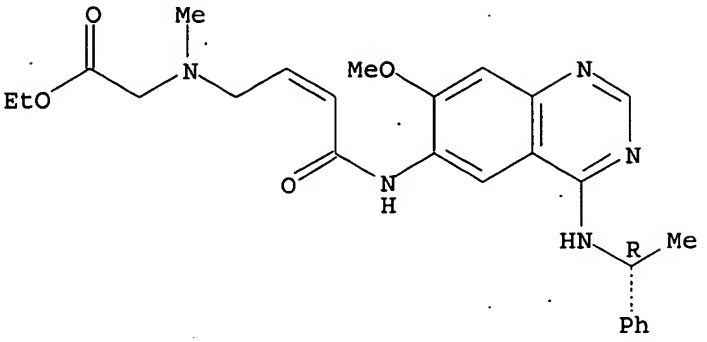


RN 290301-88-1 CAPLUS

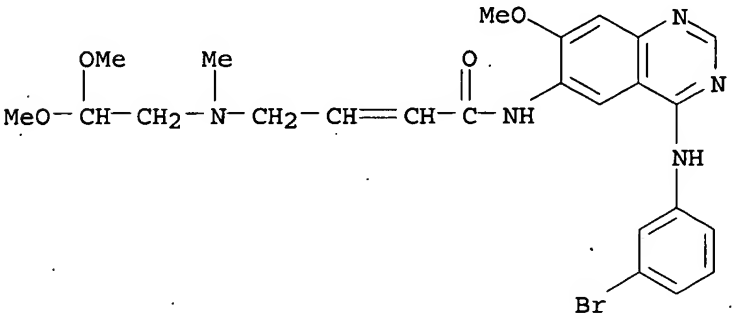
CN Glycine, N-[4-[[7-methoxy-4-[[(1R)-1-phenylethyl]amino]-6-quinazolinyl]amino]-4-oxo-2-butenyl]-N-methyl-, ethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

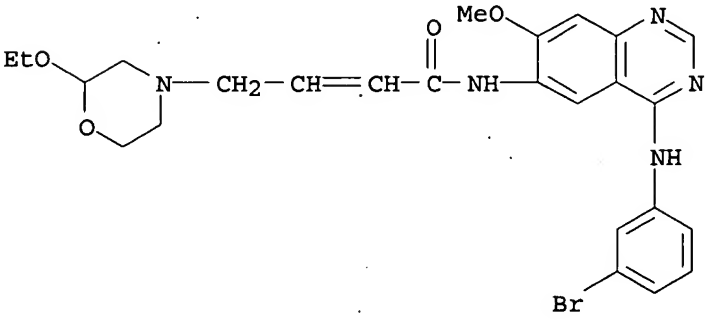
Double bond geometry unknown.



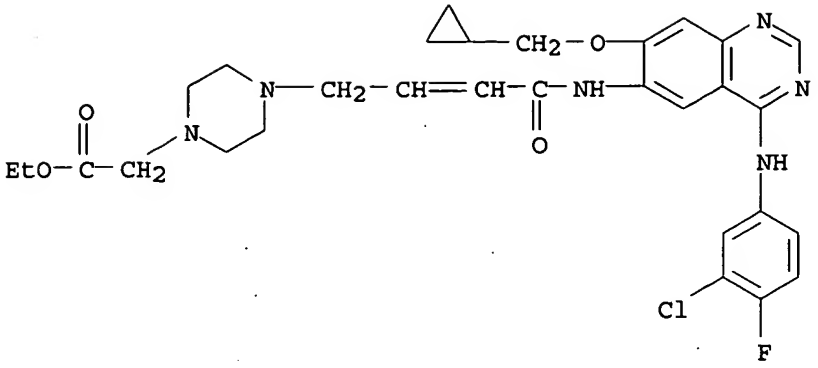
RN 290301-94-9 CAPLUS
CN 2-Butenamide, N-[4-[(3-bromophenyl)amino]-7-methoxy-6-quinazolinyl]-4-[(2,2-dimethoxyethyl)methylamino]- (9CI) (CA INDEX NAME)



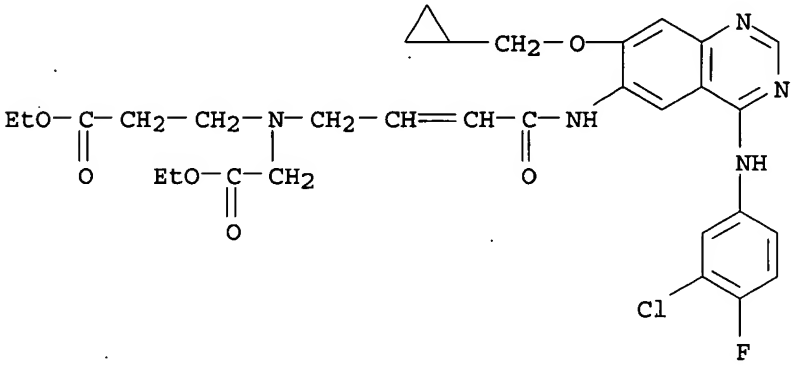
RN 290301-96-1 CAPLUS
CN 2-Butenamide, N-[4-[(3-bromophenyl)amino]-7-methoxy-6-quinazolinyl]-4-(2-ethoxy-4-morpholinyl)- (9CI) (CA INDEX NAME)



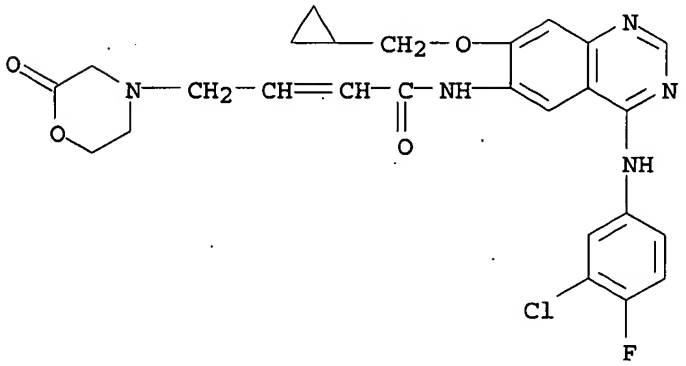
RN 290302-11-3 CAPLUS
CN 1-Piperazineacetic acid, 4-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]amino]-4-oxo-2-butenyl]-, ethyl ester (9CI) (CA INDEX NAME)



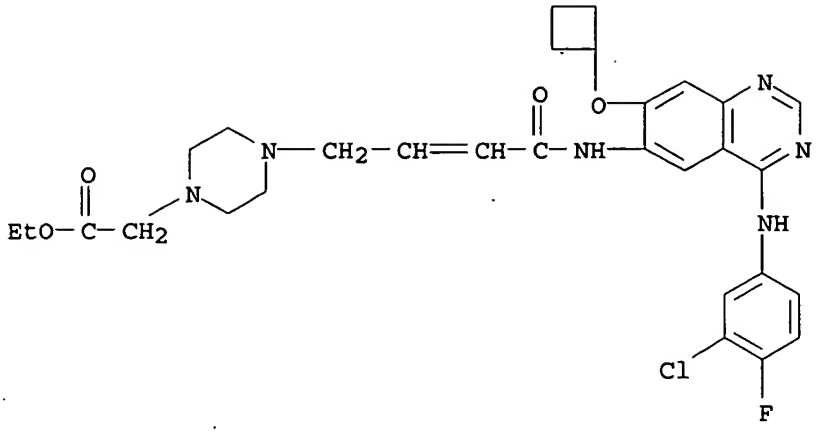
RN 290302-19-1 CAPLUS
CN .beta.-Alanine, N-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]amino]-4-oxo-2-butenyl]-N-(2-ethoxy-2-oxoethyl)-, ethyl ester (9CI) (CA INDEX NAME)



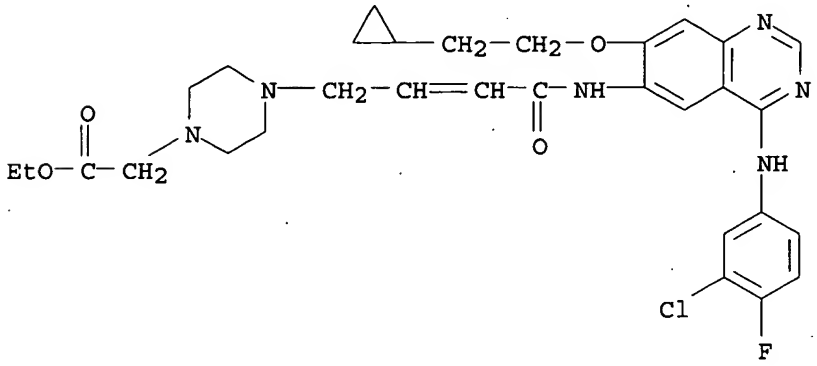
RN 290302-25-9 CAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-(2-oxo-4-morpholinyl)- (9CI) (CA INDEX NAME)



RN 290302-33-9 CAPLUS
CN 1-Piperazineacetic acid, 4-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclobutyloxy)-6-quinazolinyl]amino]-4-oxo-2-butenyl]-, ethyl ester (9CI) (CA INDEX NAME)

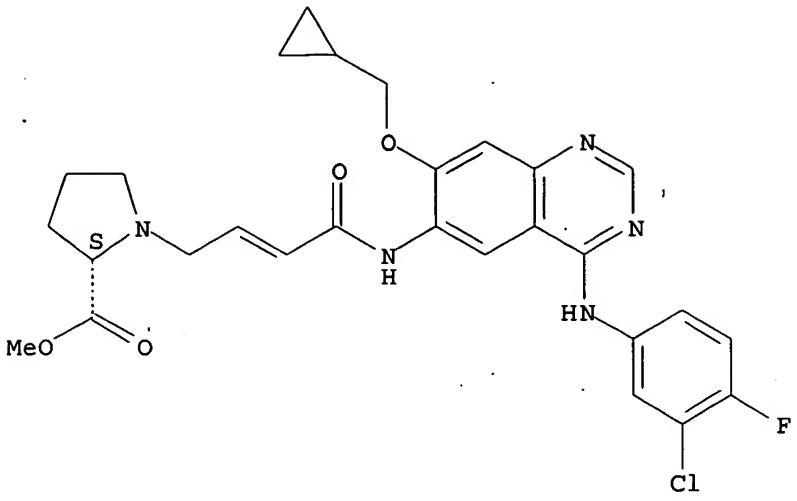


RN 290302-39-5 CAPLUS
CN 1-Piperazineacetic acid, 4-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(2-cyclopropylethoxy)-6-quinazolinyl]amino]-4-oxo-2-butenyl]-, ethyl ester (9CI) (CA INDEX NAME)

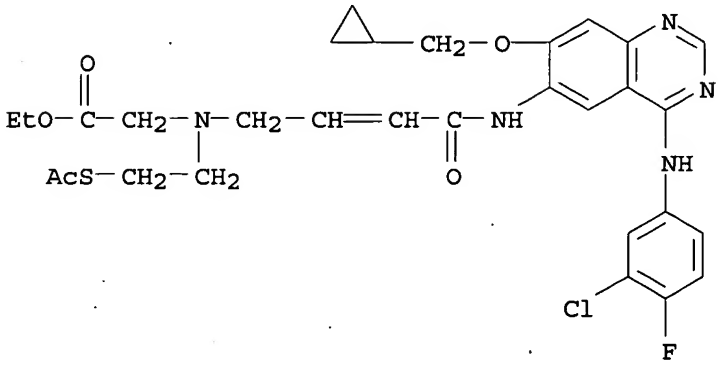


RN 290302-47-5 CAPLUS
CN L-Proline, 1-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]amino]-4-oxo-2-butenyl]-, methyl ester (9CI) (CA INDEX NAME)

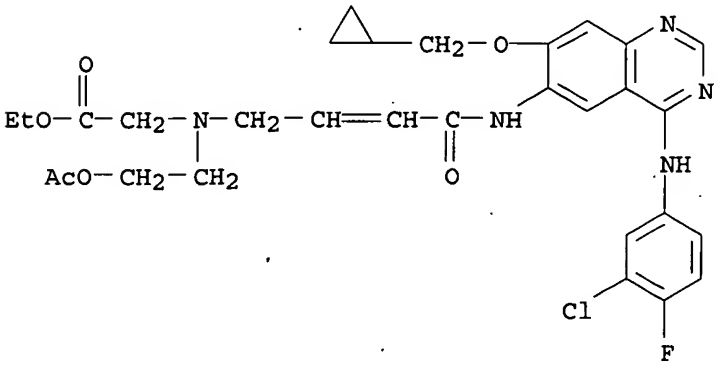
Absolute stereochemistry.
Double bond geometry unknown.



RN 290302-98-6 CAPLUS
CN Glycine, N-[2-(acetylthio)ethyl]-N-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]amino]-4-oxo-2-butenyl]-, ethyl ester (9CI) (CA INDEX NAME)



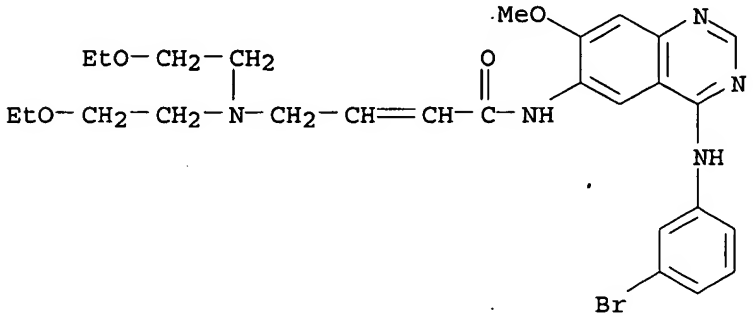
RN 290303-04-7 CAPLUS
CN Glycine, N-[2-(acetyloxy)ethyl]-N-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]amino]-4-oxo-2-butenyl]-, ethyl ester (9CI) (CA INDEX NAME)



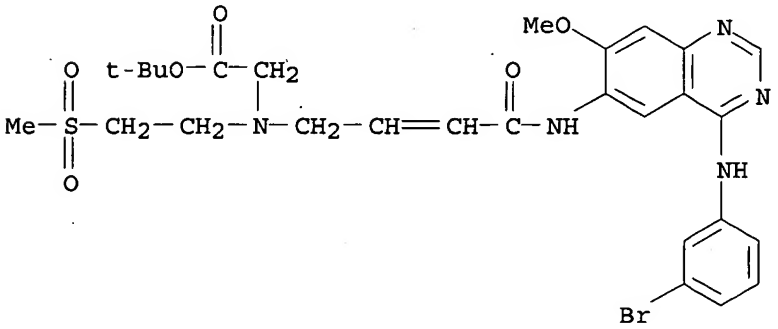
10/ 023,099

IT **290304-09-5 290304-10-8**
RL: RCT (Reactant); RACT (Reactant or reagent)
(prepn. of aminoquinazoline and aminoquinoline derivs. having an inhibitory effect on signal transduction mediated by tyrosine kinases useful for treating tumoral diseases, lung and respiratory tract diseases)

RN 290304-09-5 CAPLUS
CN 2-Butenamide, 4-[bis(2-ethoxyethyl)amino]-N-[4-[(3-bromophenyl)amino]-7-methoxy-6-quinazolinyl]- (9CI) (CA INDEX NAME)

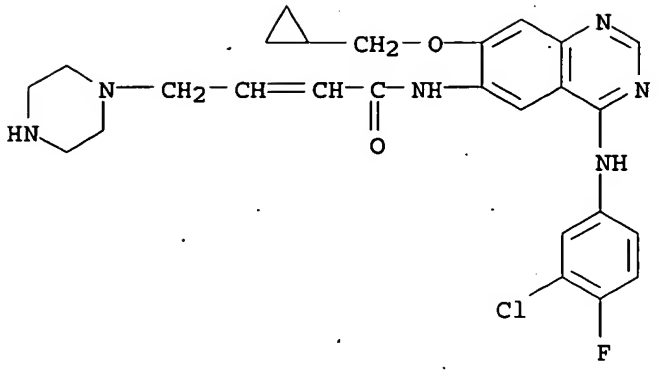


RN 290304-10-8 CAPLUS
CN Glycine, N-[4-[[4-[(3-bromophenyl)amino]-7-methoxy-6-quinazolinyl]amino]-4-oxo-2-butenyl]-N-[2-(methylsulfonyl)ethyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

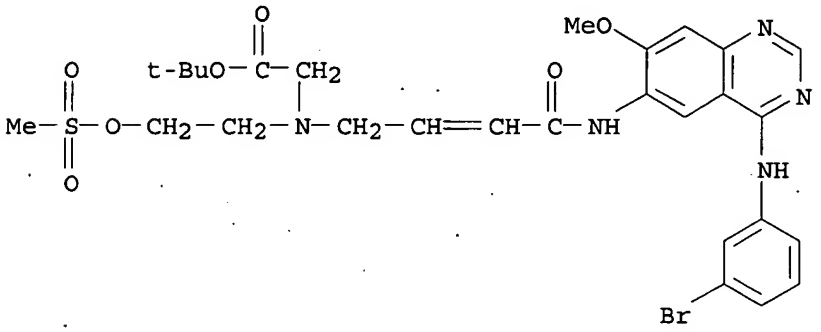


IT **290303-47-8P 290303-83-2P 290303-84-3P**
290304-01-7P 290304-02-8P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of aminoquinazoline and aminoquinoline derivs. having an inhibitory effect on signal transduction mediated by tyrosine kinases useful for treating tumoral diseases, lung and respiratory tract diseases)

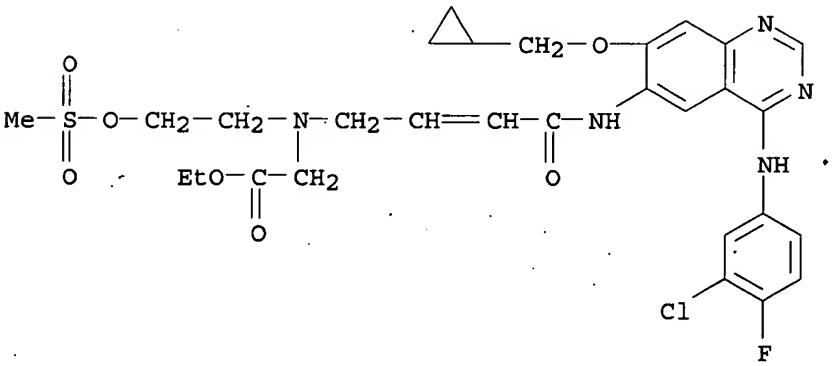
RN 290303-47-8 CAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-(1-piperazinyl)- (9CI) (CA INDEX NAME)



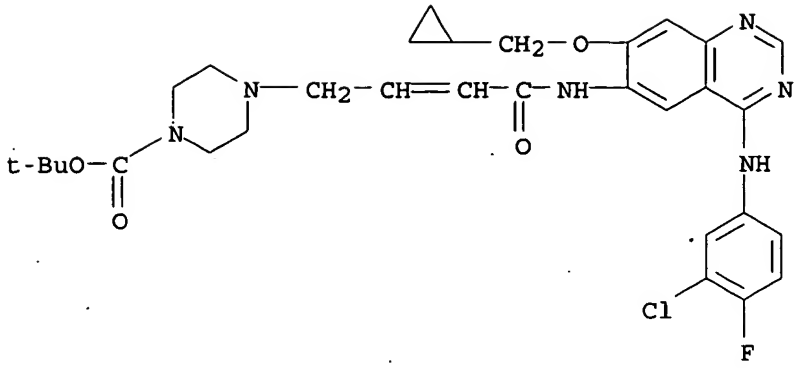
RN 290303-83-2 CAPLUS
CN Glycine, N-[4-[[4-[(3-bromophenyl)amino]-7-methoxy-6-quinazolinyl]amino]-4-oxo-2-butenyl]-N-[2-[(methylsulfonyl)oxy]ethyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



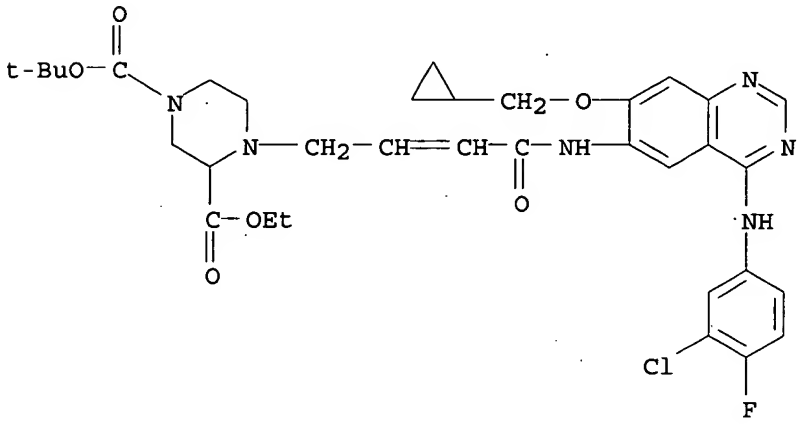
RN 290303-84-3 CAPLUS
CN Glycine, N-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]amino]-4-oxo-2-butenyl]-N-[2-[(methylsulfonyl)oxy]ethyl]-, ethyl ester (9CI) (CA INDEX NAME)



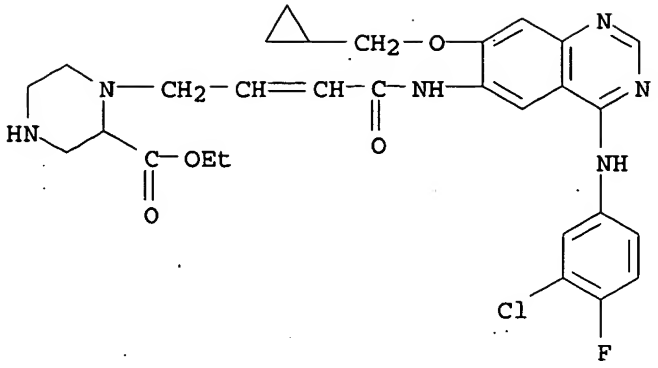
RN 290304-01-7 CAPLUS
CN 1-Piperazinecarboxylic acid, 4-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]amino]-4-oxo-2-butenyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



RN 290304-02-8 CAPLUS
CN 1,3-Piperazinedicarboxylic acid, 4-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]amino]-4-oxo-2-butenyl]-, 1-(1,1-dimethylethyl) 3-ethyl ester (9CI) (CA INDEX NAME)



IT **290303-13-8P**
RL: RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(prepn. of aminoquinazoline and aminoquinoline derivs. having an inhibitory effect on signal transduction mediated by tyrosine kinases useful for treating tumoral diseases, lung and respiratory tract diseases)
RN 290303-13-8 CAPLUS
CN 2-Piperazinecarboxylic acid, 1-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]amino]-4-oxo-2-butenyl]-, ethyl ester (9CI) (CA INDEX NAME)



IT **289700-69-2P 290301-73-4P 290301-74-5P**
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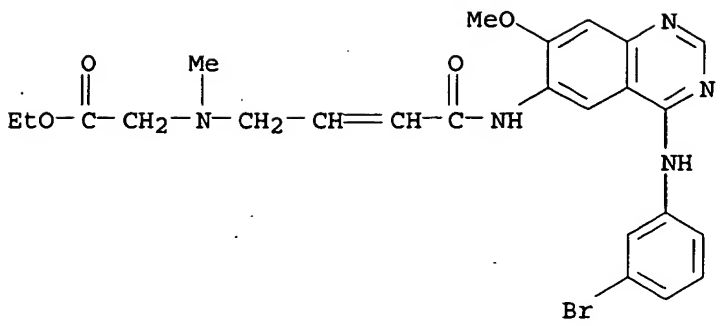
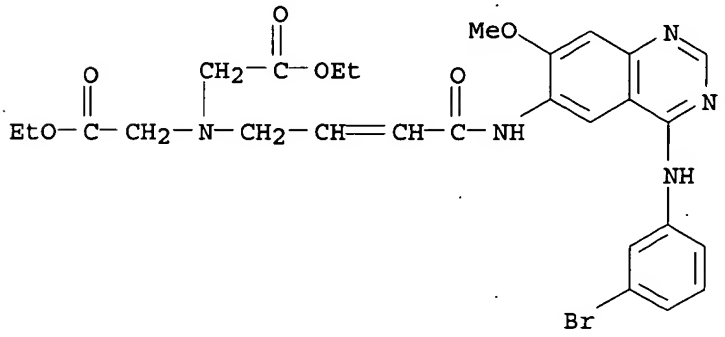
290303-15-0P 290303-16-1P 290303-17-2P
290303-18-3P
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of aminoquinazoline and aminoquinoline derivs. having an inhibitory effect on signal transduction mediated by tyrosine kinases useful for treating tumoral diseases, lung and respiratory tract diseases)

RN 289700-69-2 CAPLUS

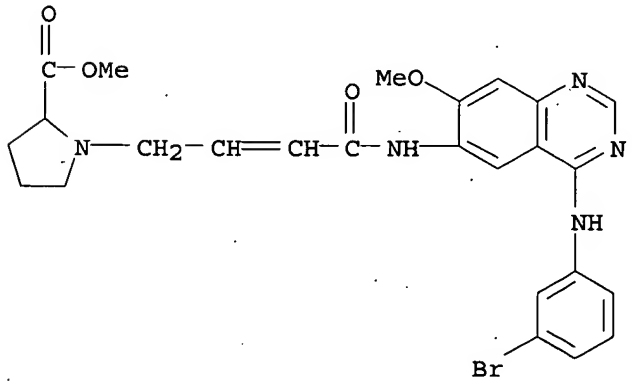
CN Glycine, N-[4-[[4-[(3-bromophenyl)amino]-7-methoxy-6-quinazolinyl]amino]-4-oxo-2-butenyl]-N-methyl-, ethyl ester (9CI) (CA INDEX NAME)



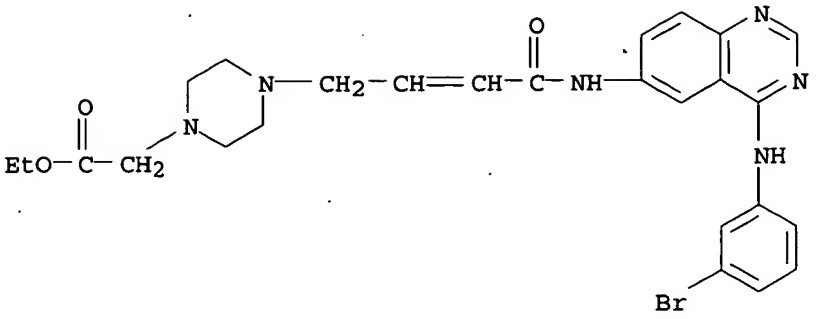
RN 290301-73-4 CAPLUS
CN Glycine, N-[4-[[4-[(3-bromophenyl)amino]-7-methoxy-6-quinazolinyl]amino]-4-oxo-2-butenyl]-N-(2-ethoxy-2-oxoethyl)-, ethyl ester (9CI) (CA INDEX NAME)



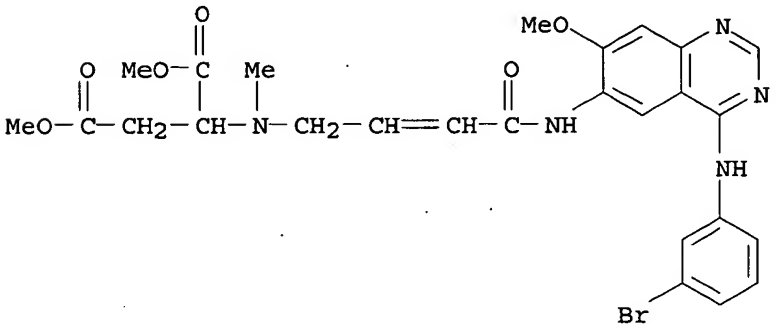
RN 290301-74-5 CAPLUS
CN Proline, 1-[4-[[4-[(3-bromophenyl)amino]-7-methoxy-6-quinazolinyl]amino]-4-oxo-2-butenyl]-, methyl ester (9CI) (CA INDEX NAME)



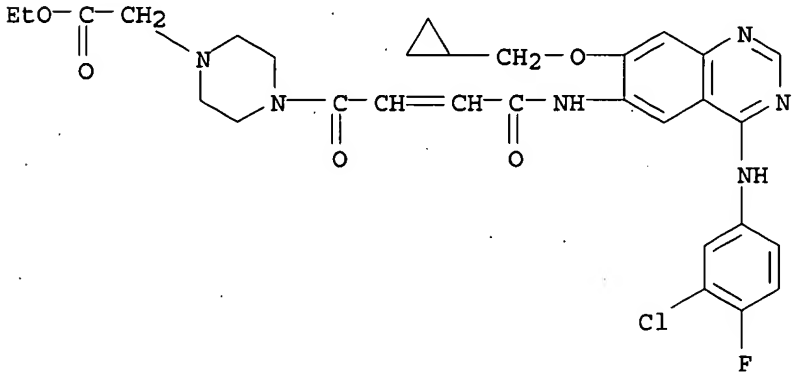
RN 290301-76-7 CAPLUS
CN 1-Piperazineacetic acid, 4-[4-[[4-[(3-bromophenyl)amino]-6-quinazolinyl]amino]-4-oxo-2-butenyl]-, ethyl ester (9CI) (CA INDEX NAME)



RN 290301-77-8 CAPLUS
CN Aspartic acid, N-[4-[[4-[(3-bromophenyl)amino]-7-methoxy-6-quinazolinyl]amino]-4-oxo-2-butenyl]-N-methyl-, dimethyl ester (9CI) (CA INDEX NAME)



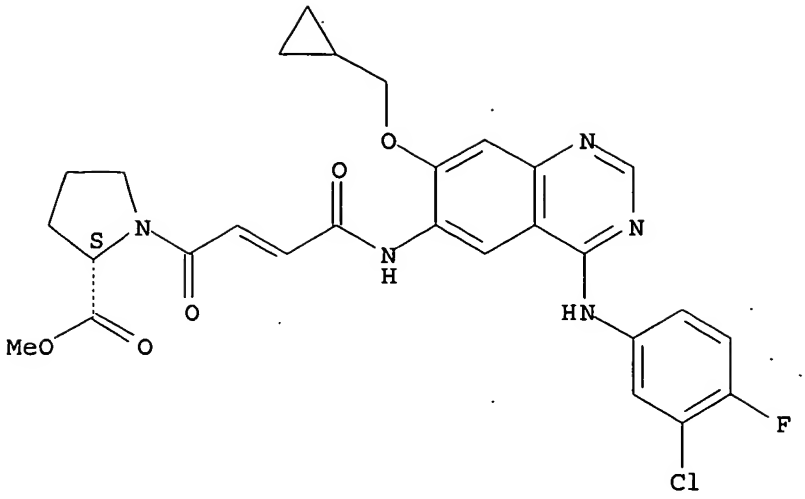
RN 290301-81-4 CAPLUS
CN 1-Piperazineacetic acid, 4-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]amino]-1,4-dioxo-2-butenyl]-, ethyl ester (9CI) (CA INDEX NAME)



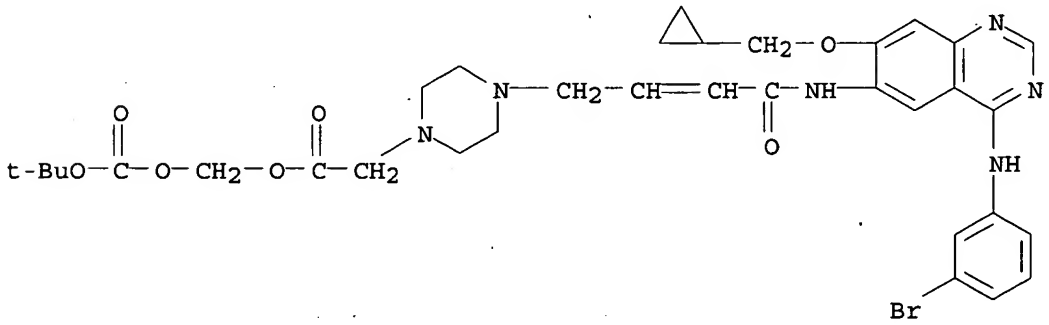
RN 290301-82-5 CAPLUS
CN L-Proline, 1-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]amino]-1,4-dioxo-2-butenyl]-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.

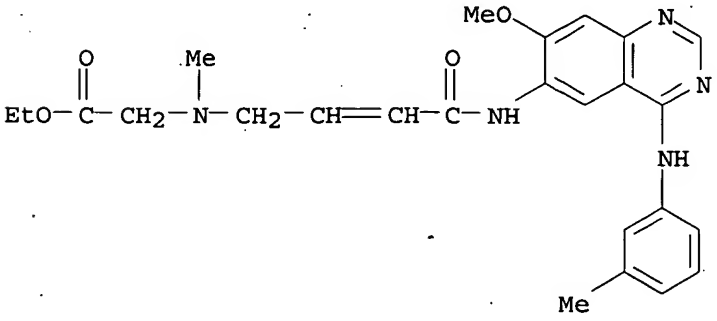
10/ 023,099



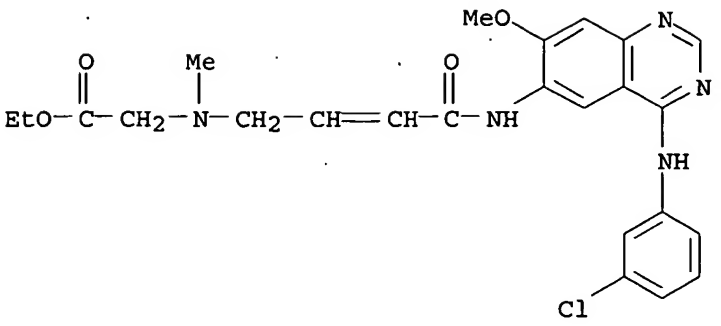
RN 290301-85-8 CAPLUS
CN 1-Piperazineacetic acid, 4-[4-[[4-[(3-bromophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]amino]-4-oxo-2-butenyl]-, [[(1,1-dimethylethoxy)carbonyl]oxy]methyl ester (9CI) (CA INDEX NAME)



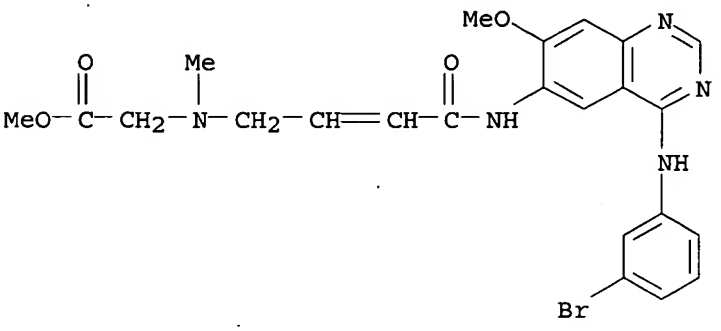
RN 290301-86-9 CAPLUS
CN Glycine, N-[4-[[7-methoxy-4-[(3-methylphenyl)amino]-6-quinazolinyl]amino]-4-oxo-2-butenyl]-N-methyl-, ethyl ester (9CI) (CA INDEX NAME)



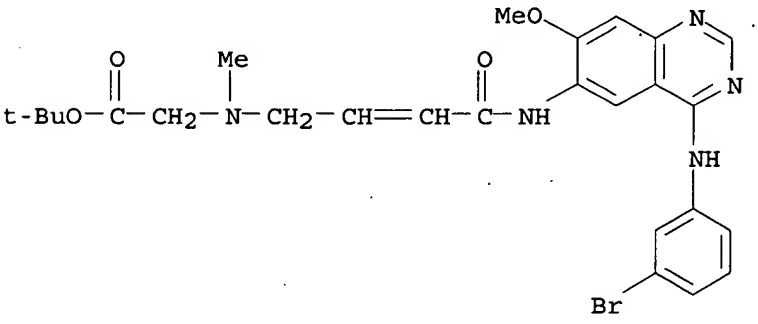
RN 290301-87-0 CAPLUS
CN Glycine, N-[4-[[4-[(3-chlorophenyl)amino]-7-methoxy-6-quinazolinyl]amino]-4-oxo-2-butenyl]-N-methyl-, ethyl ester (9CI) (CA INDEX NAME)



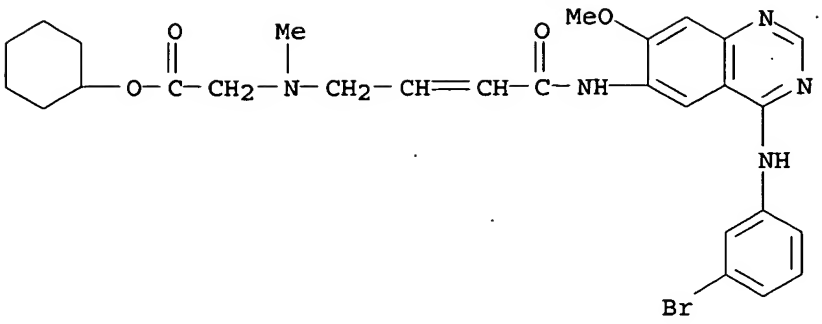
RN 290301-89-2 CAPLUS
CN Glycine, N-[4-[[4-[(3-bromophenyl)amino]-7-methoxy-6-quinazolinyl]amino]-4-oxo-2-butenyl]-N-methyl-, methyl ester (9CI) (CA INDEX NAME)



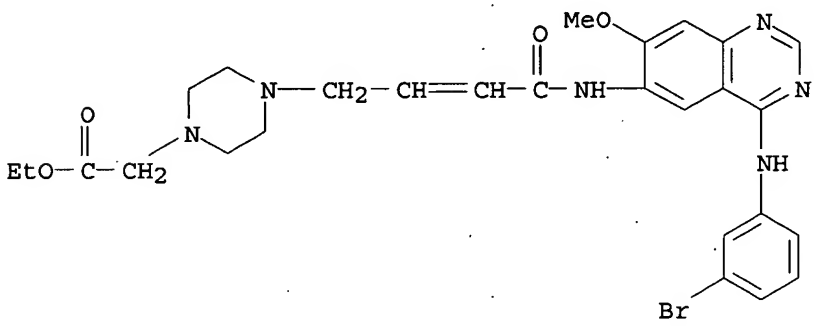
RN 290301-90-5 CAPLUS
CN Glycine, N-[4-[[4-[(3-bromophenyl)amino]-7-methoxy-6-quinazolinyl]amino]-4-oxo-2-butenyl]-N-methyl-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



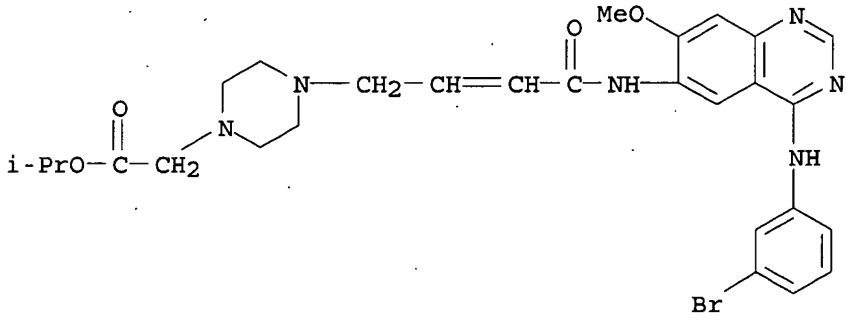
RN 290301-91-6 CAPLUS
CN Glycine, N-[4-[[4-[(3-bromophenyl)amino]-7-methoxy-6-quinazolinyl]amino]-4-oxo-2-butenyl]-N-methyl-, cyclohexyl ester (9CI) (CA INDEX NAME)



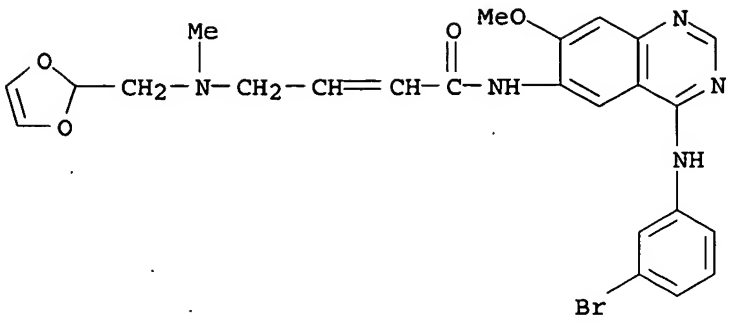
RN 290301-92-7 CAPLUS
CN 1-Piperazineacetic acid, 4-[4-[[4-[(3-bromophenyl)amino]-7-methoxy-6-quinazolinyl]amino]-4-oxo-2-butenyl]-, ethyl ester (9CI) (CA INDEX NAME)



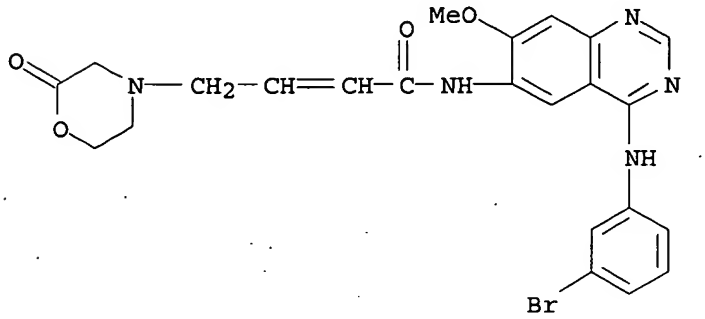
RN 290301-93-8 CAPLUS
CN 1-Piperazineacetic acid, 4-[4-[[4-[(3-bromophenyl)amino]-7-methoxy-6-quinazolinyl]amino]-4-oxo-2-butenyl]-, 1-methylethyl ester (9CI) (CA INDEX NAME)



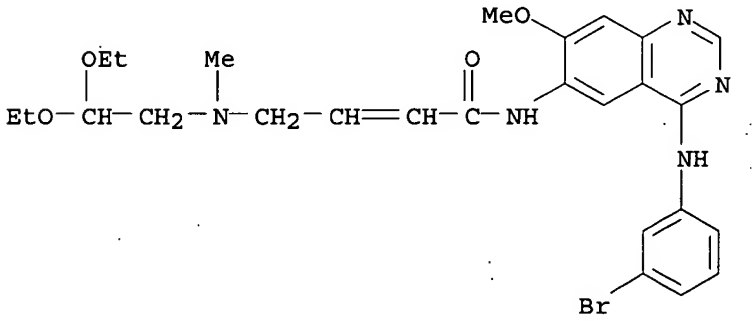
RN 290301-95-0 CAPLUS
CN 2-Butenamide, N-[4-[(3-bromophenyl)amino]-7-methoxy-6-quinazolinyl]-4-[(1,3-dioxol-2-ylmethyl)methylamino]- (9CI) (CA INDEX NAME)



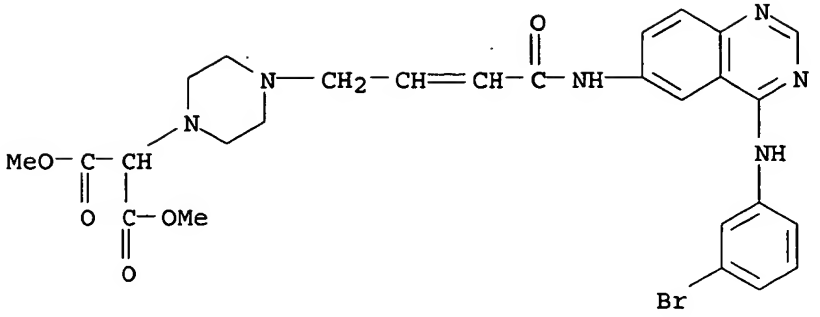
RN 290301-98-3 CAPLUS
CN 2-Butenamide, N-[4-[(3-bromophenyl)amino]-7-methoxy-6-quinazolinyl]-4-(2-oxo-4-morpholinyl)- (9CI) (CA INDEX NAME)



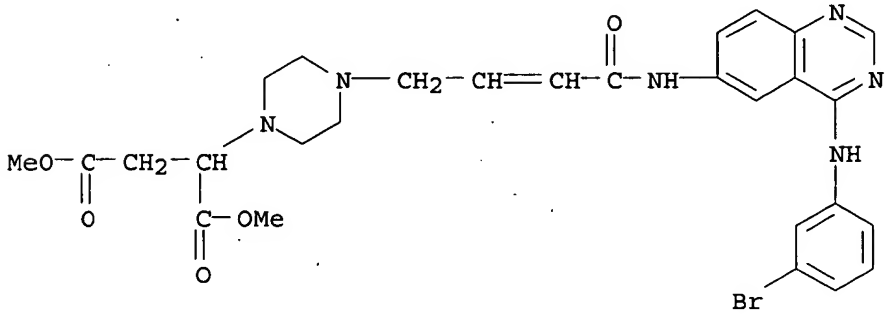
RN 290302-01-1 CAPLUS
CN 2-Butenamide, N-[4-[(3-bromophenyl)amino]-7-methoxy-6-quinazolinyl]-4-[(2,2-diethoxyethyl)methylamino]- (9CI) (CA INDEX NAME)



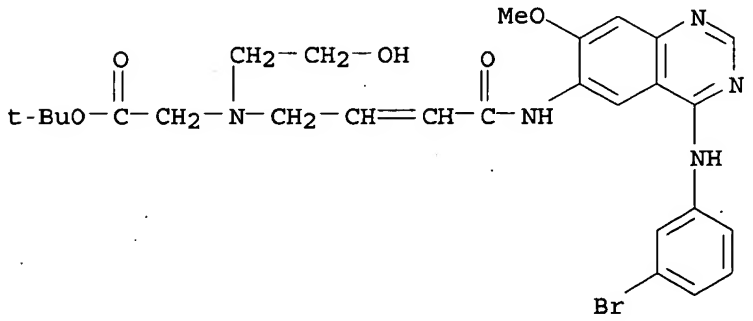
RN 290302-03-3 CAPLUS
CN Propanedioic acid, [4-[4-[[4-[(3-bromophenyl)amino]-6-quinazolinyl]amino]-4-oxo-2-butenyl]-1-piperazinyl]-, dimethyl ester (9CI) (CA INDEX NAME)



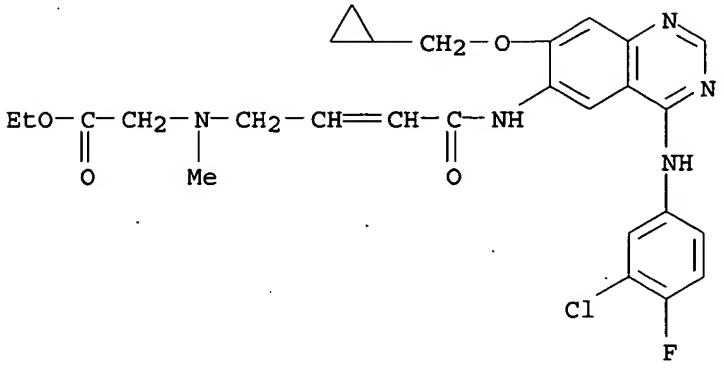
RN 290302-05-5 CAPLUS
CN Butanedioic acid, [4-[4-[[4-[(3-bromophenyl)amino]-6-quinazolinyl]amino]-4-oxo-2-butenyl]-1-piperazinyl]-, dimethyl ester (9CI) (CA INDEX NAME)



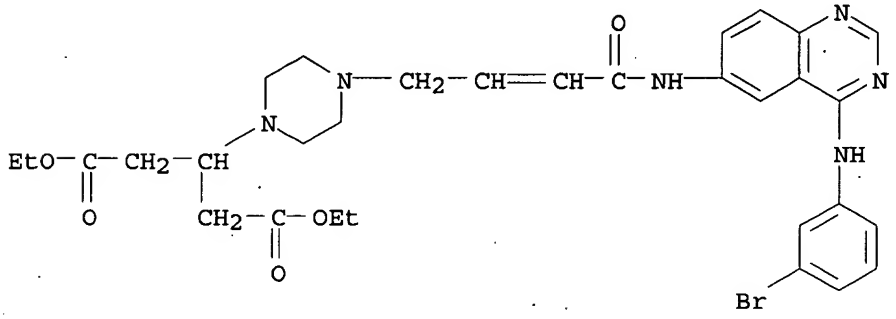
RN 290302-07-7 CAPLUS
CN Glycine, N-[4-[[4-[(3-bromophenyl)amino]-7-methoxy-6-quinazolinyl]amino]-4-oxo-2-butenyl]-N-(2-hydroxyethyl)-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



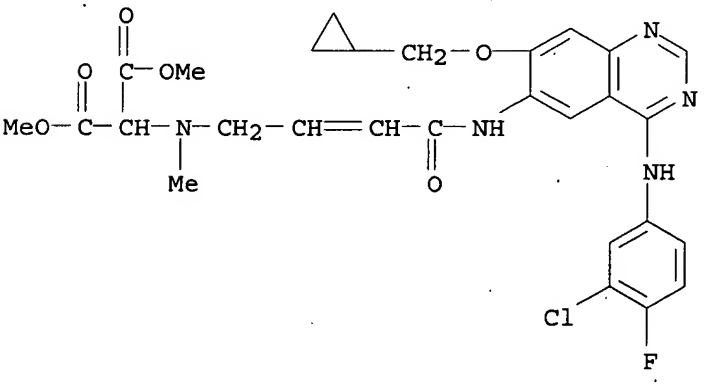
RN 290302-09-9 CAPLUS
CN Glycine, N-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]amino]-4-oxo-2-butenyl]-N-methyl-, ethyl ester (9CI) (CA INDEX NAME)



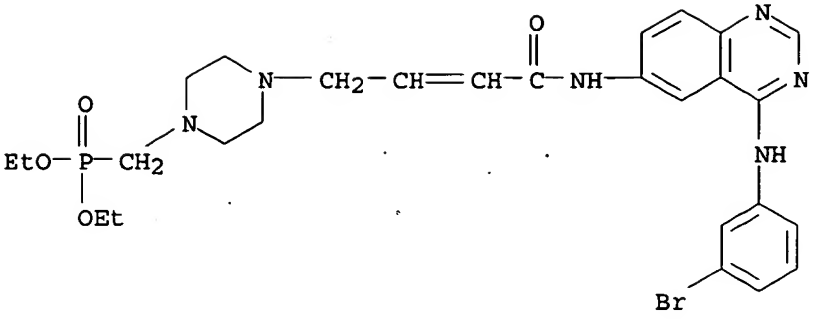
RN 290302-13-5 CAPLUS
CN Pentanedioic acid, 3-[4-[4-[[4-[(3-bromophenyl)amino]-6-quinazolinyl]amino]-4-oxo-2-butenyl]-1-piperazinyl]-, diethyl ester (9CI) (CA INDEX NAME)



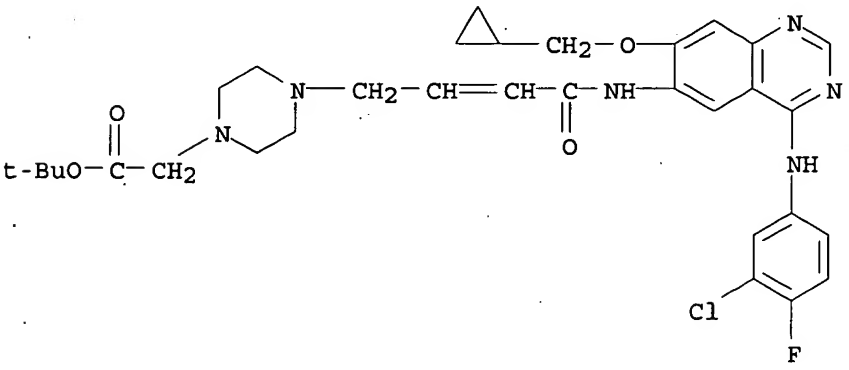
RN 290302-15-7 CAPLUS
CN Propanedioic acid, [[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]amino]-4-oxo-2-butenyl]methylamino]-, dimethyl ester (9CI) (CA INDEX NAME)



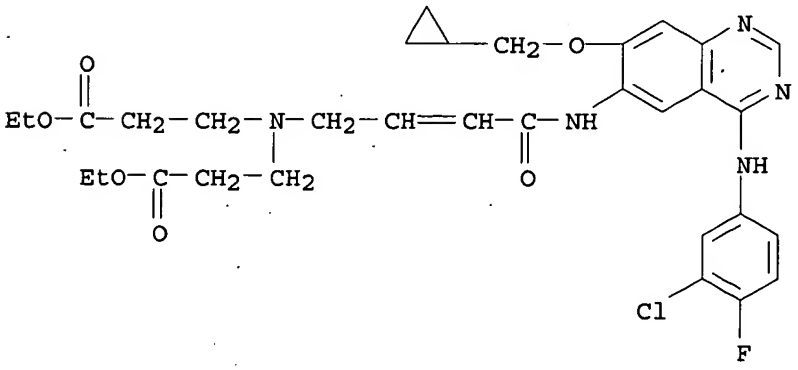
RN 290302-17-9 CAPLUS
CN Phosphonic acid, [[4-[4-[[4-[(3-bromophenyl)amino]-6-quinazolinyl]amino]-4-oxo-2-butenyl]-1-piperazinyl]methyl]-, diethyl ester (9CI) (CA INDEX NAME)



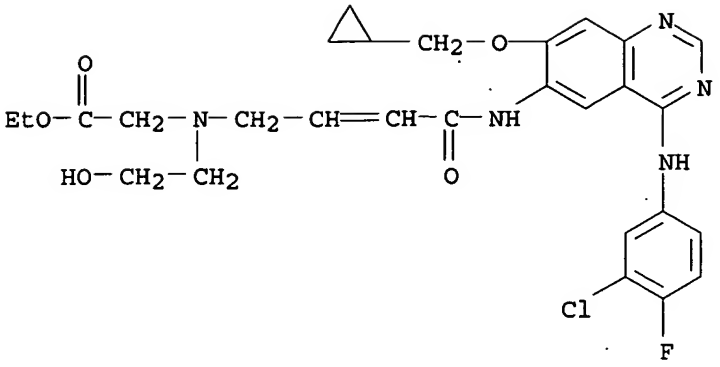
RN 290302-21-5 CAPLUS
CN 1-Piperazineacetic acid, 4-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]amino]-4-oxo-2-butenyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



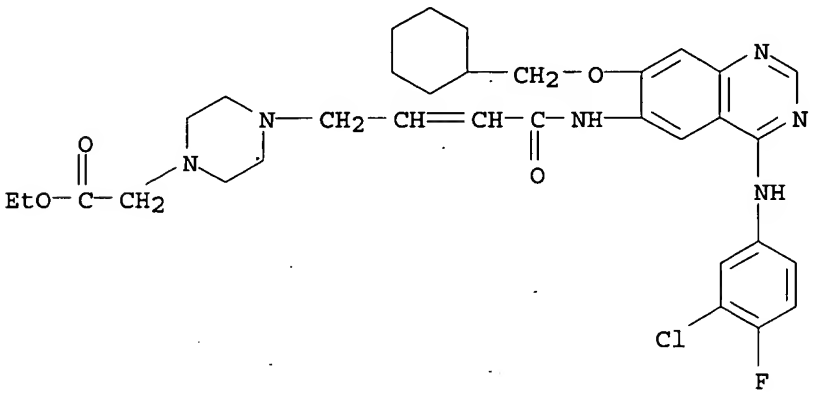
RN 290302-23-7 CAPLUS
CN .beta.-Alanine, N-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]amino]-4-oxo-2-butenyl]-N-(3-ethoxy-3-oxopropyl)-, ethyl ester (9CI) (CA INDEX NAME)



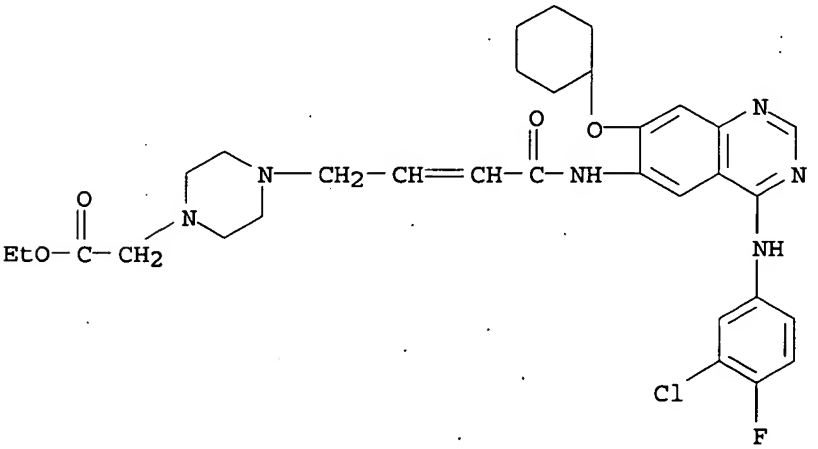
RN 290302-27-1 CAPLUS
CN Glycine, N-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]amino]-4-oxo-2-butenyl]-N-(2-hydroxyethyl)-, ethyl ester (9CI) (CA INDEX NAME)



RN 290302-29-3 CAPLUS
CN 1-Piperazineacetic acid, 4-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclohexylmethoxy)-6-quinazolinyl]amino]-4-oxo-2-butenyl]-, ethyl ester (9CI) (CA INDEX NAME)



RN 290302-31-7 CAPLUS
CN 1-Piperazineacetic acid, 4-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclohexyloxy)-6-quinazolinyl]amino]-4-oxo-2-butenyl]-, ethyl ester (9CI) (CA INDEX NAME)



RN 290302-35-1 CAPLUS

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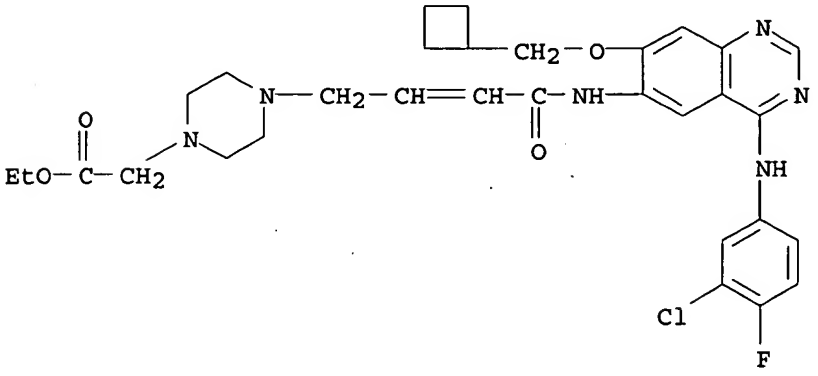
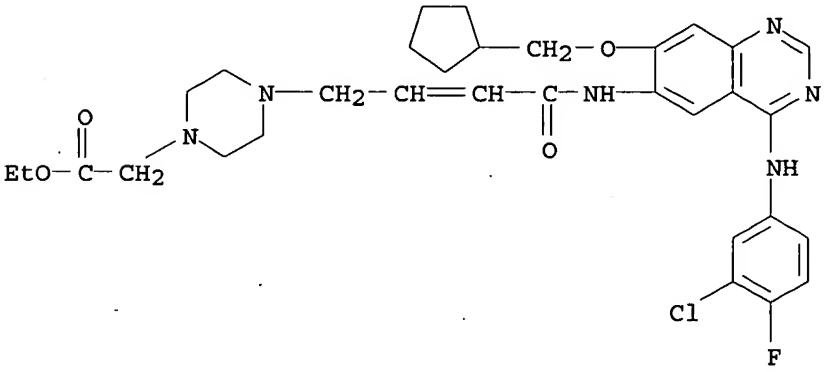
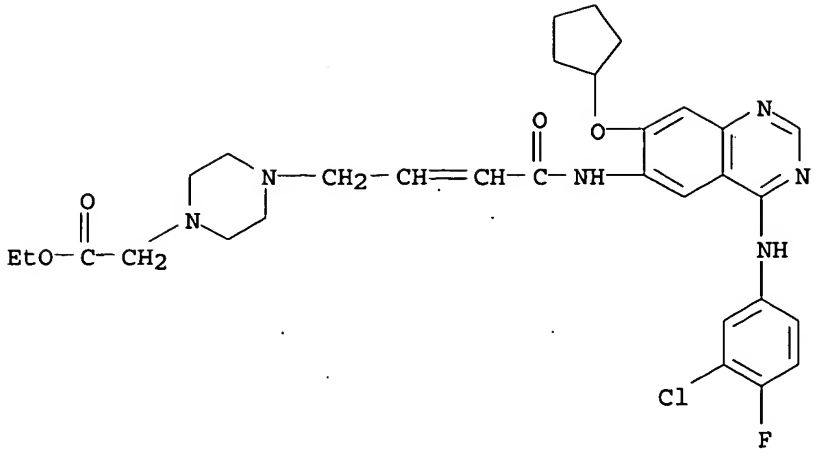
CN 1-Piperazineacetic acid, 4-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclobutylmethoxy)-6-quinazolinyl]amino]-4-oxo-2-butenyl]-, ethyl ester (9CI) (CA INDEX NAME)



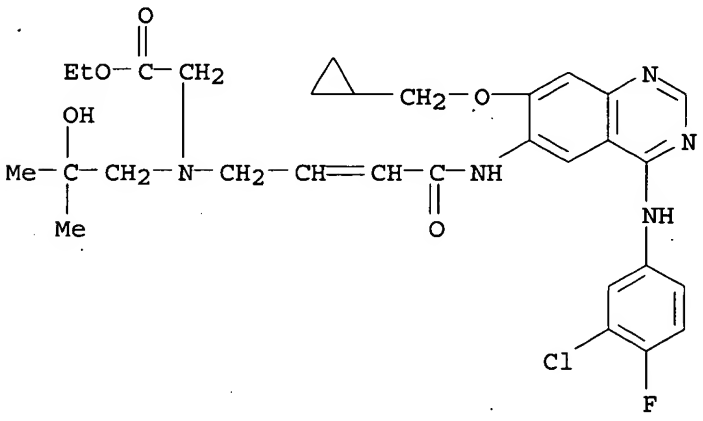
RN 290302-37-3 CAPLUS
CN 1-Piperazineacetic acid, 4-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopentylmethoxy)-6-quinazolinyl]amino]-4-oxo-2-butenyl]-, ethyl ester (9CI) (CA INDEX NAME)



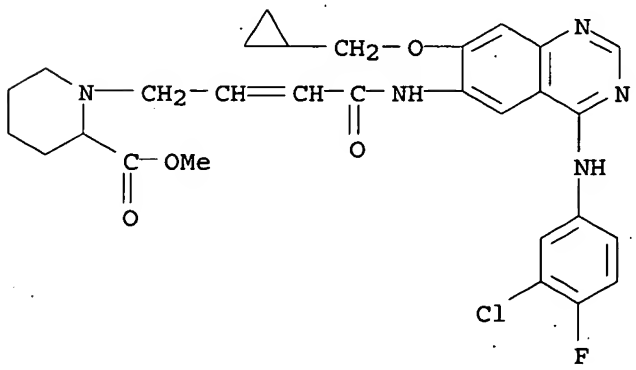
RN 290302-41-9 CAPLUS
CN 1-Piperazineacetic acid, 4-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopentyloxy)-6-quinazolinyl]amino]-4-oxo-2-butenyl]-, ethyl ester (9CI) (CA INDEX NAME)



RN 290302-43-1 CAPLUS
CN Glycine, N-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]amino]-4-oxo-2-butenyl]-N-(2-hydroxy-2-methylpropyl)-, ethyl ester (9CI) (CA INDEX NAME)



RN 290302-45-3 CAPLUS
CN 2-Piperidinecarboxylic acid, 1-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]amino]-4-oxo-2-butenyl]-, methyl ester (9CI) (CA INDEX NAME)



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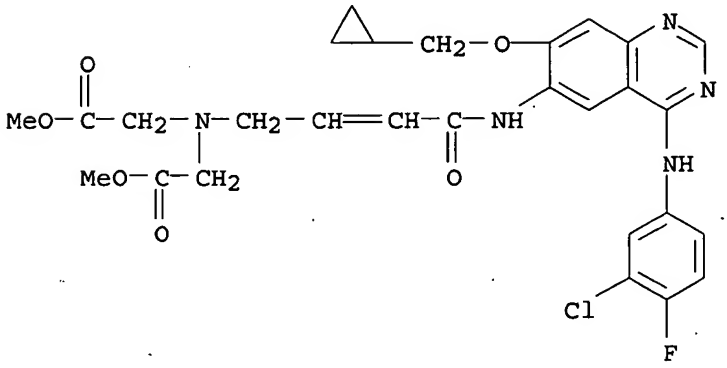
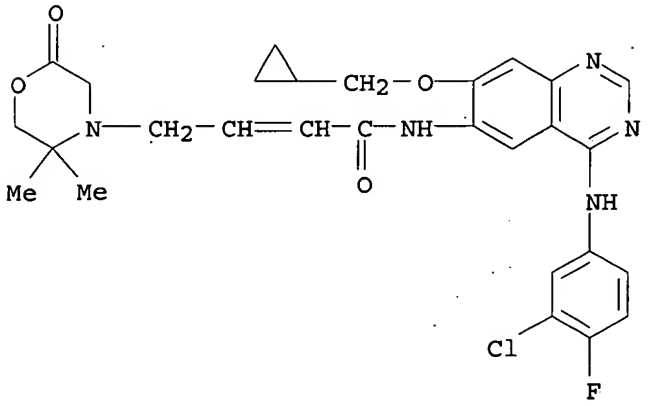
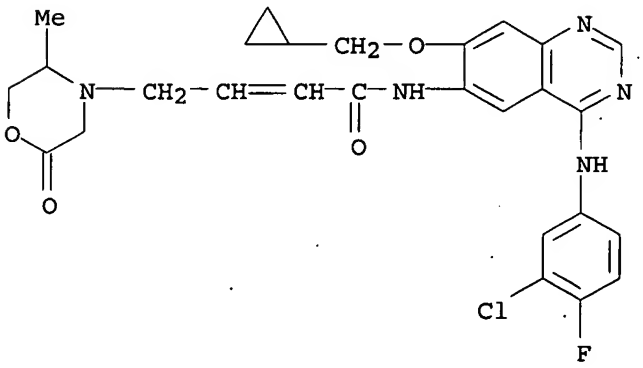
RN 290302-49-7 CAPLUS
CN Glycine, N-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]amino]-4-oxo-2-butenyl]-N-(2-methoxy-2-oxoethyl)-, methyl ester (9CI) (CA INDEX NAME)



RN 290302-51-1 CAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-(5,5-dimethyl-2-oxo-4-morpholinyl)- (9CI) (CA INDEX NAME)



RN 290302-53-3 CAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-(5-methyl-2-oxo-4-morpholinyl)- (9CI) (CA INDEX NAME)



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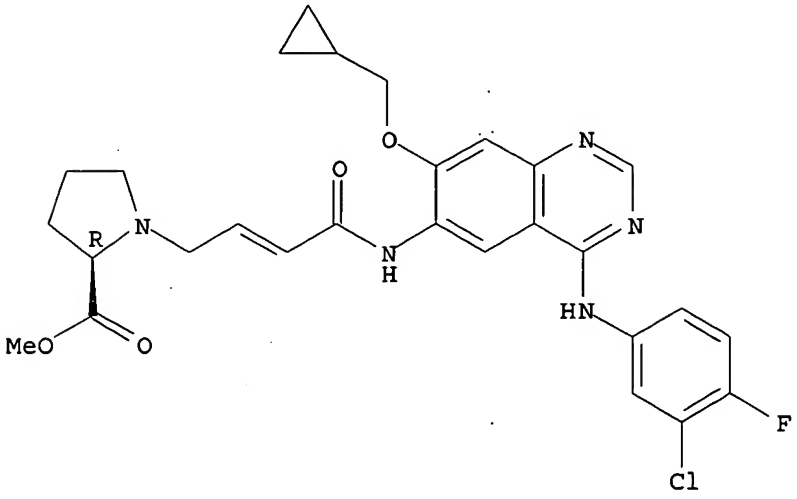
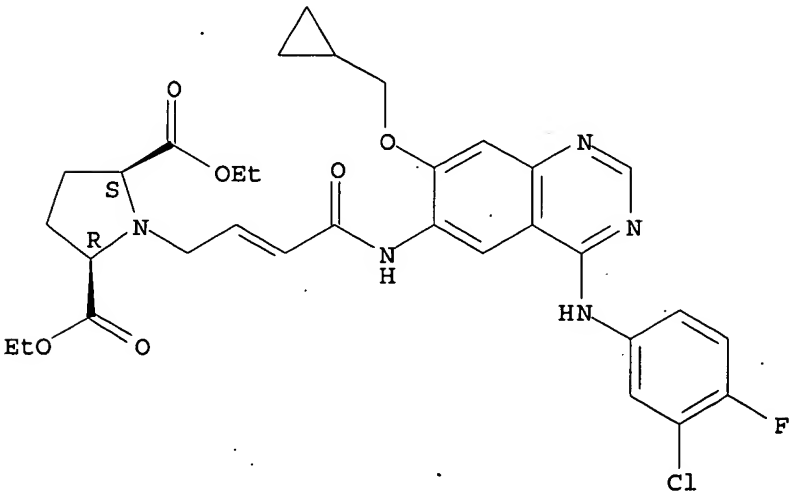
RN 290302-55-5 CAPLUS
CN D-Proline, 1-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]amino]-4-oxo-2-butenyl]-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



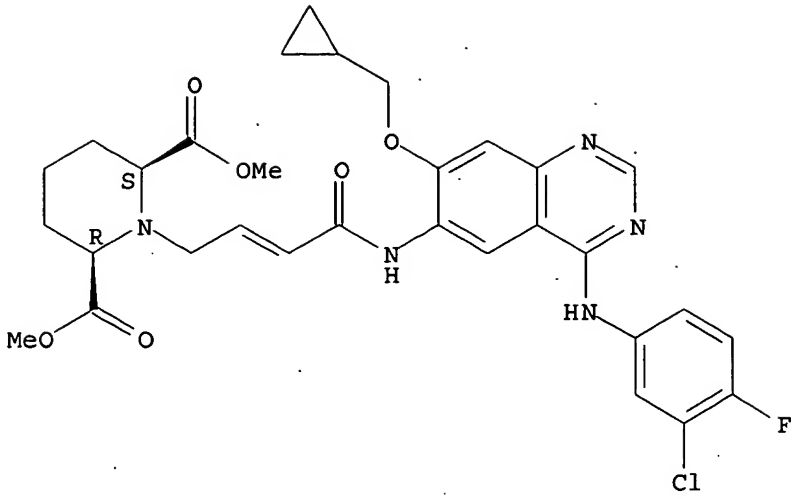
RN 290302-57-7 CAPLUS
CN 2,5-Pyrrolidinedicarboxylic acid, 1-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]amino]-4-oxo-2-butenyl]-, diethyl ester, (2R,5S)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.
Double bond geometry unknown.



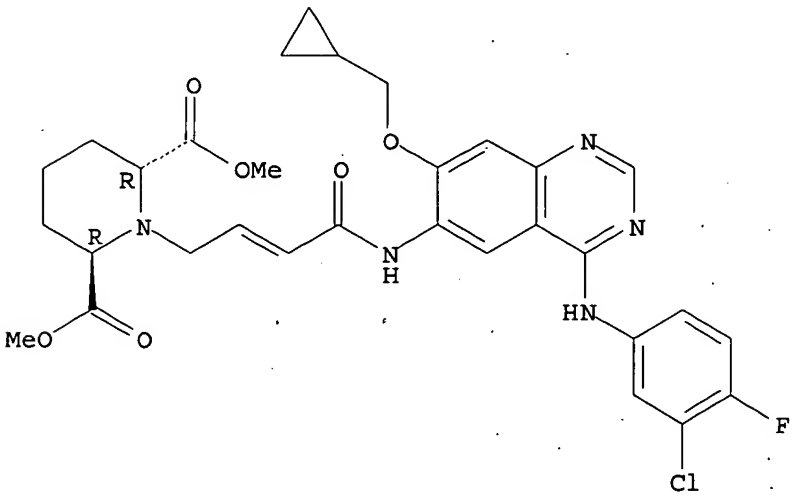
RN 290302-59-9 CAPLUS
CN 2,6-Piperidinedicarboxylic acid, 1-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]amino]-4-oxo-2-butenyl]-, dimethyl ester, (2R,6S)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.
Double bond geometry unknown.



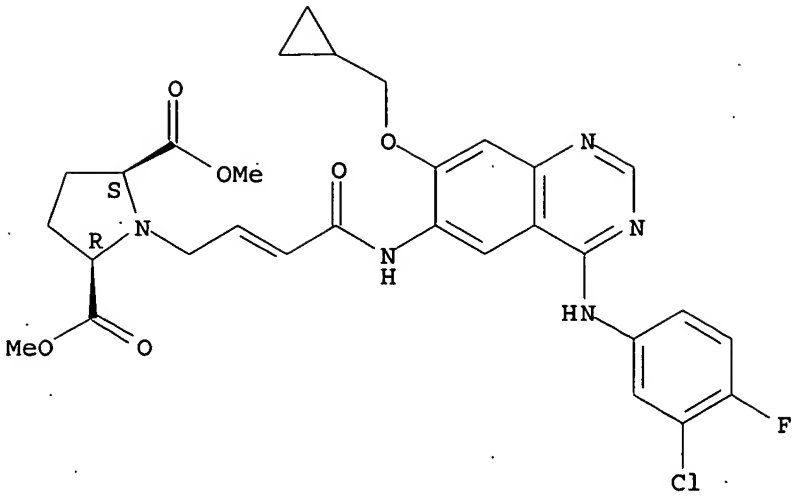
RN 290302-61-3 CAPLUS
CN 2,6-Piperidinedicarboxylic acid, 1-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]amino]-4-oxo-2-butenyl]-, dimethyl ester, (2R,6R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.
Double bond geometry unknown.



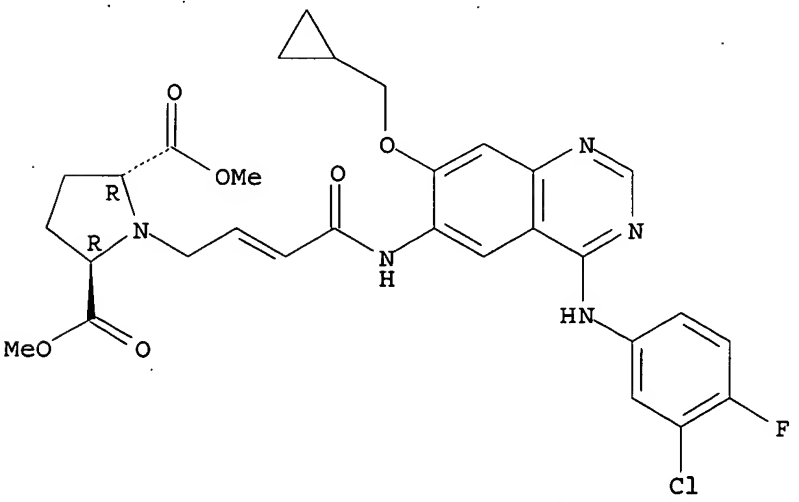
RN 290302-63-5 CAPLUS
CN 2,5-Pyrrolidinedicarboxylic acid, 1-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]amino]-4-oxo-2-butenyl]-, dimethyl ester, (2R,5S)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.
Double bond geometry unknown.

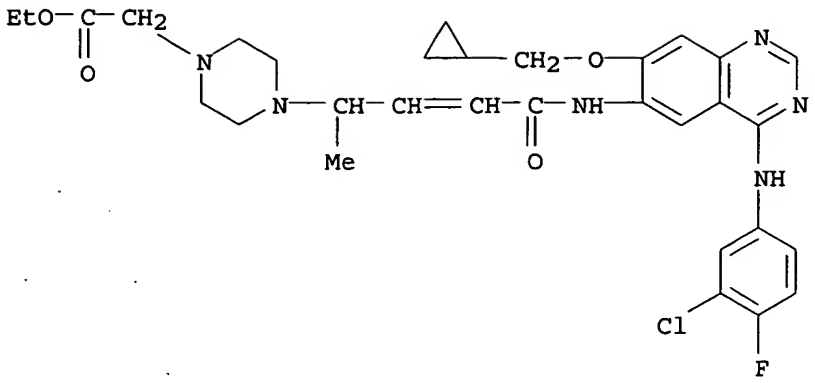


RN 290302-65-7 CAPLUS
CN 2,5-Pyrrolidinedicarboxylic acid, 1-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]amino]-4-oxo-2-butenyl]-, dimethyl ester, (2R,5R)-rel- (9CI) (CA INDEX NAME)

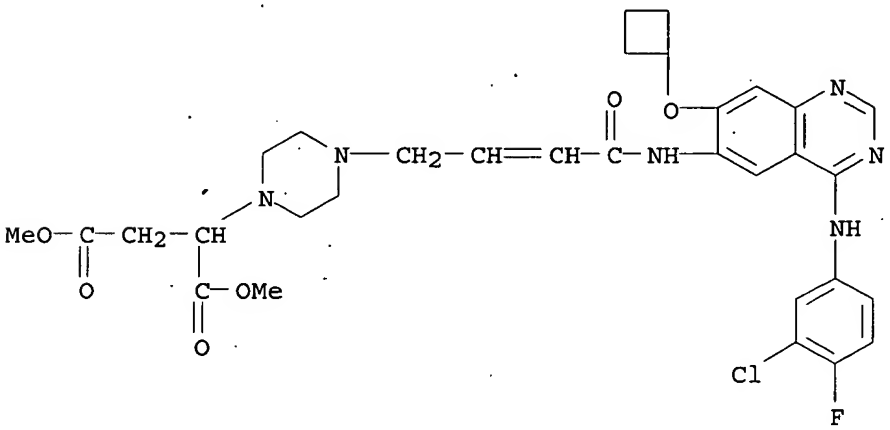
Relative stereochemistry.
Double bond geometry unknown.



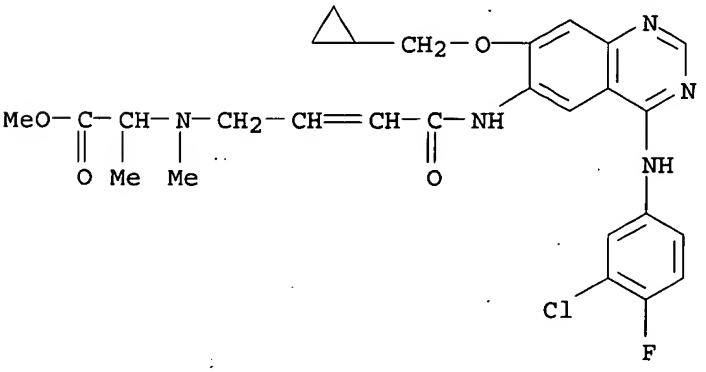
RN 290302-67-9 CAPLUS
CN 1-Piperazineacetic acid, 4-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]amino]-1-methyl-4-oxo-2-butenyl]-, ethyl ester (9CI) (CA INDEX NAME)



RN 290302-69-1 CAPLUS
CN Butanedioic acid, [4-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclobutyloxy)-6-quinazolinyl]amino]-4-oxo-2-butenyl]-1-piperazinyl]-, dimethyl ester (9CI) (CA INDEX NAME)



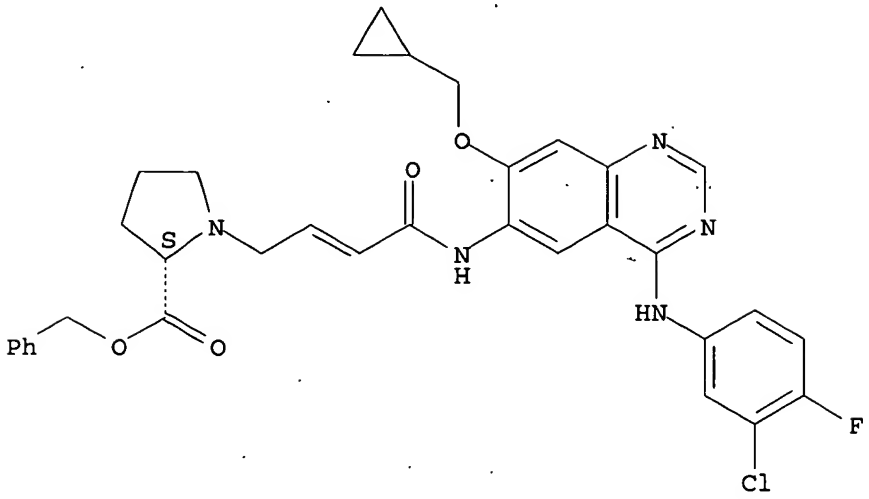
RN 290302-71-5 CAPLUS
CN Alanine, N-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]amino]-4-oxo-2-butenyl]-N-methyl-, methyl ester (9CI) (CA INDEX NAME)



RN 290302-73-7 CAPLUS
CN L-Proline, 1-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]amino]-4-oxo-2-butenyl]-, phenylmethyl

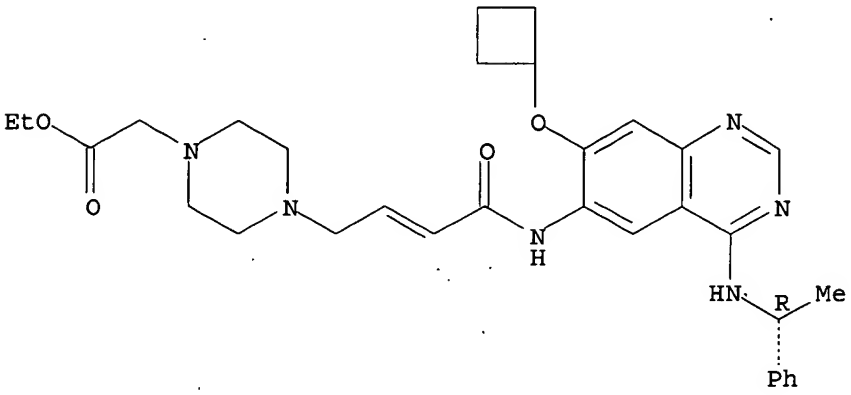
ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



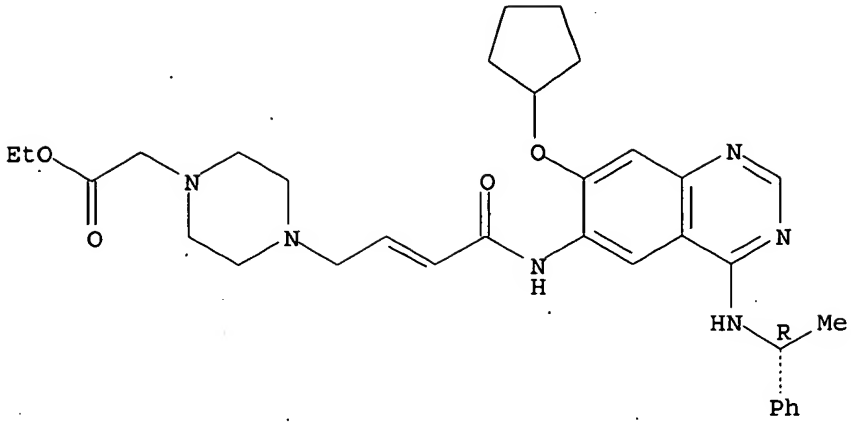
RN 290302-75-9 CAPLUS
CN 1-Piperazineacetic acid, 4-[4-[[7-(cyclobutyloxy)-4-[[(1R)-1-phenylethyl]amino]-6-quinazolinyl]amino]-4-oxo-2-butenyl]-, ethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



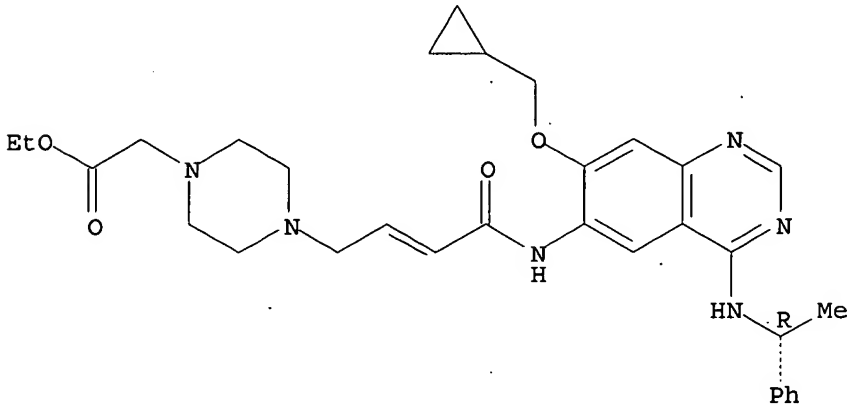
RN 290302-77-1 CAPLUS
CN 1-Piperazineacetic acid, 4-[4-[[7-(cyclopentyloxy)-4-[[(1R)-1-phenylethyl]amino]-6-quinazolinyl]amino]-4-oxo-2-butenyl]-, ethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.

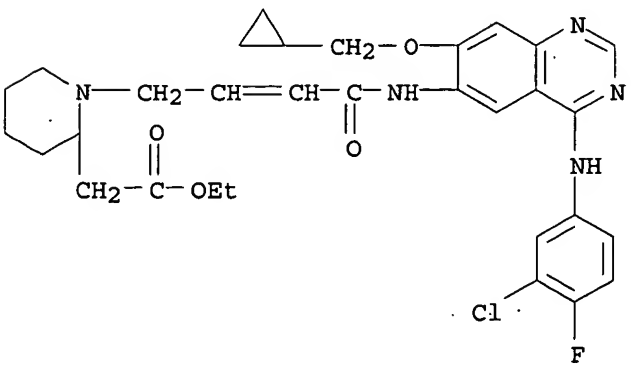


RN 290302-79-3 CAPLUS
CN 1-Piperazineacetic acid, 4-[4-[[7-(cyclopropylmethoxy)-4-[[(1R)-1-phenylethyl]amino]-6-quinazolinyl]amino]-4-oxo-2-butenyl]-, ethyl ester (9CI) (CA INDEX NAME)

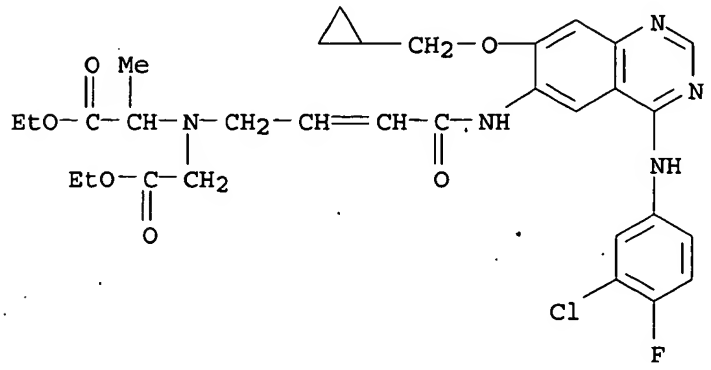
Absolute stereochemistry.
Double bond geometry unknown.



RN 290302-81-7 CAPLUS
CN 2-Piperidineacetic acid, 1-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]amino]-4-oxo-2-butenyl]-, ethyl ester (9CI) (CA INDEX NAME)

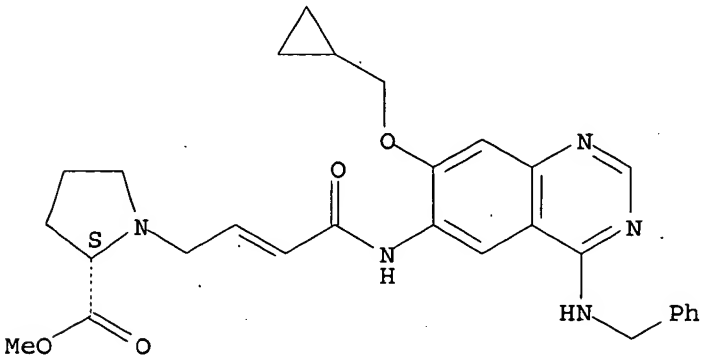


RN 290302-83-9 CAPLUS
CN Alanine, N-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]amino]-4-oxo-2-butenyl]-N-(2-ethoxy-2-oxoethyl)-, ethyl ester (9CI) (CA INDEX NAME)

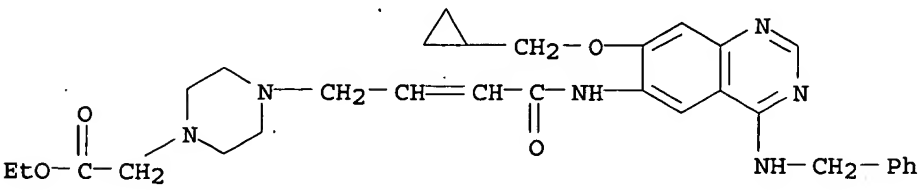


RN 290302-85-1 CAPLUS
CN L-Proline, 1-[4-[[7-(cyclopropylmethoxy)-4-[(phenylmethyl)amino]-6-quinazolinyl]amino]-4-oxo-2-butenyl]-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



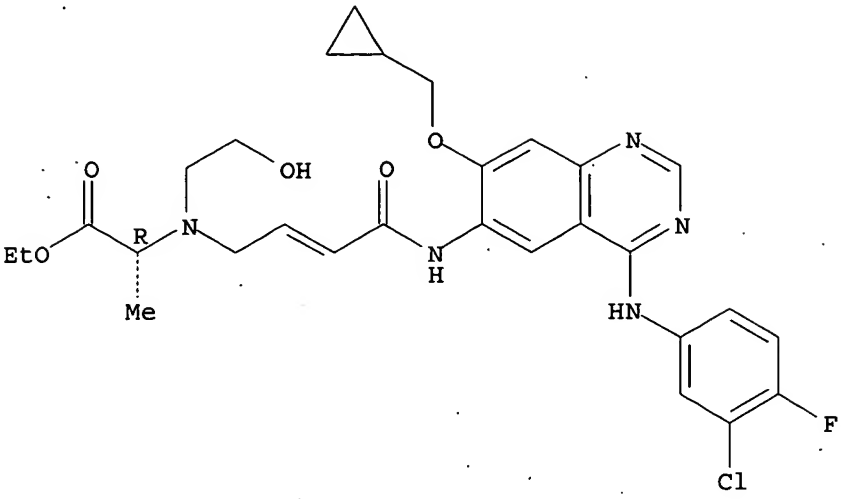
RN 290302-87-3 CAPLUS
CN 1-Piperazineacetic acid, 4-[4-[[7-(cyclopropylmethoxy)-4-[(phenylmethyl)amino]-6-quinazolinyl]amino]-4-oxo-2-butenyl]-, ethyl ester (9CI) (CA INDEX NAME)



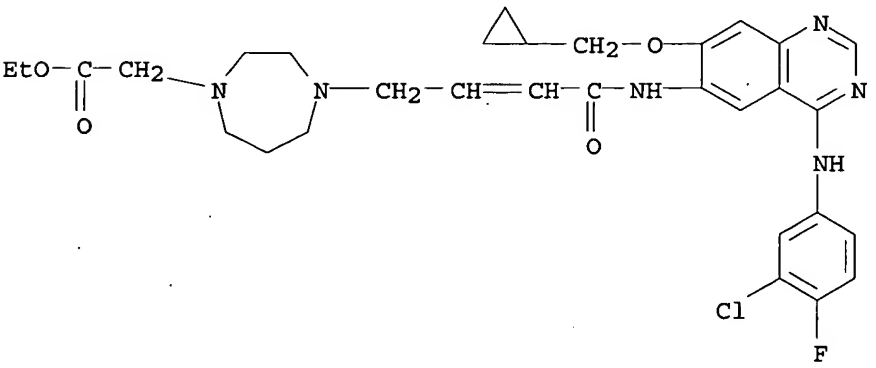
RN 290302-89-5 CAPLUS
CN D-Alanine, N-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]amino]-4-oxo-2-butenyl]-N-(2-hydroxyethyl)-, ethyl ester (9CI) (CA INDEX NAME)

10/ 023,099

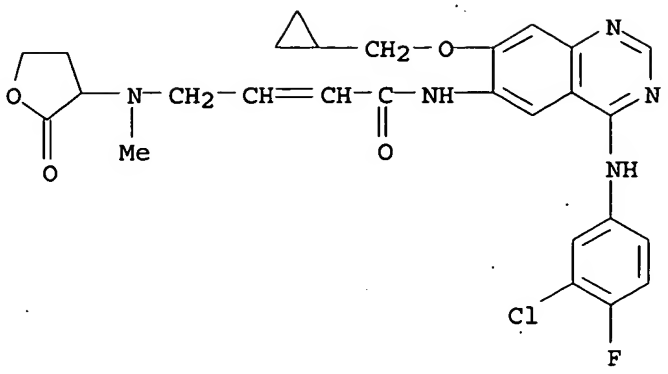
Absolute stereochemistry.
Double bond geometry unknown.



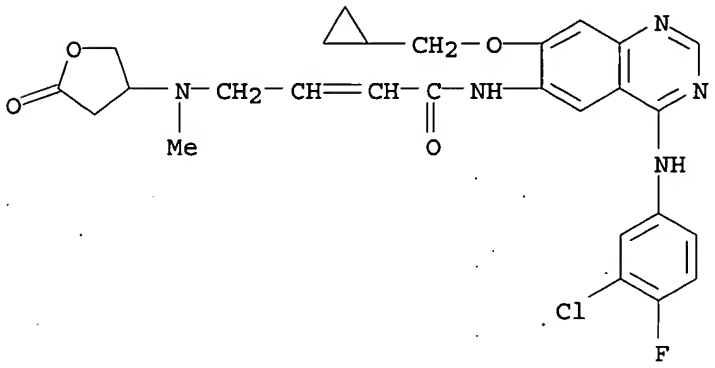
RN 290302-91-9 CAPLUS
CN 1H-1,4-Diazepine-1-acetic acid, 4-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]amino]-4-oxo-2-butenyl]hexahydro-, ethyl ester (9CI) (CA INDEX NAME)



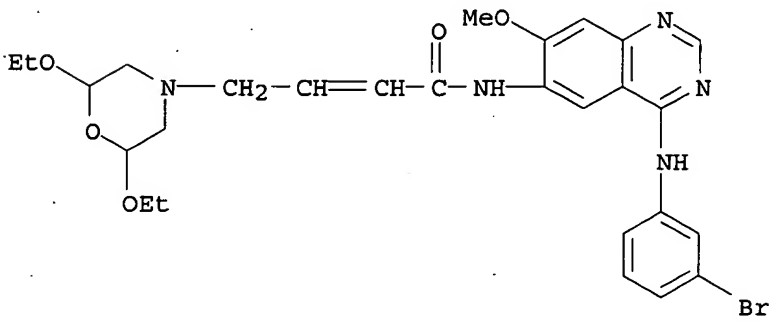
RN 290302-93-1 CAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-[methyl(tetrahydro-2-oxo-3-furanyl)amino]- (9CI) (CA INDEX NAME)



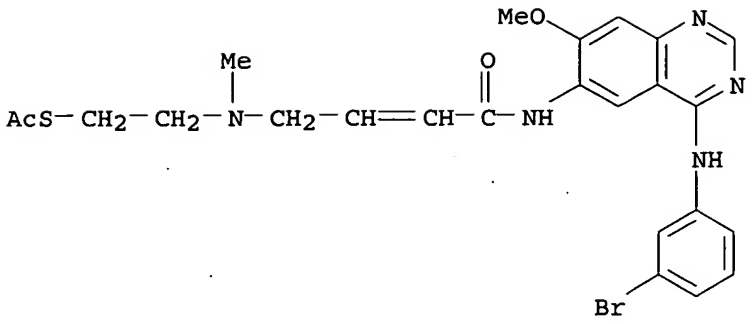
RN 290302-94-2 CAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-[methyl(tetrahydro-5-oxo-3-furanyl)amino]- (9CI) (CA INDEX NAME)



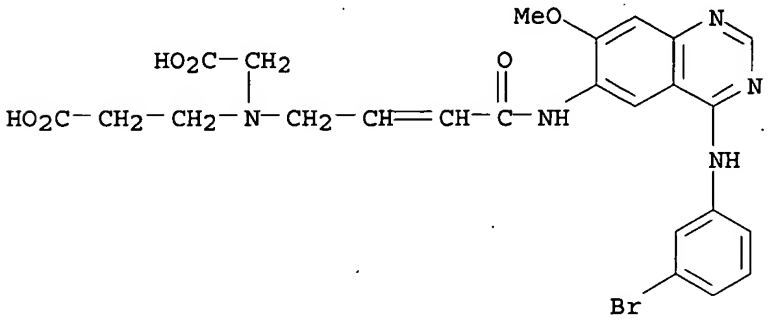
RN 290302-96-4 CAPLUS
CN 2-Butenamide, N-[4-[(3-bromophenyl)amino]-7-methoxy-6-quinazolinyl]-4-(2,6-diethoxy-4-morpholinyl)- (9CI) (CA INDEX NAME)



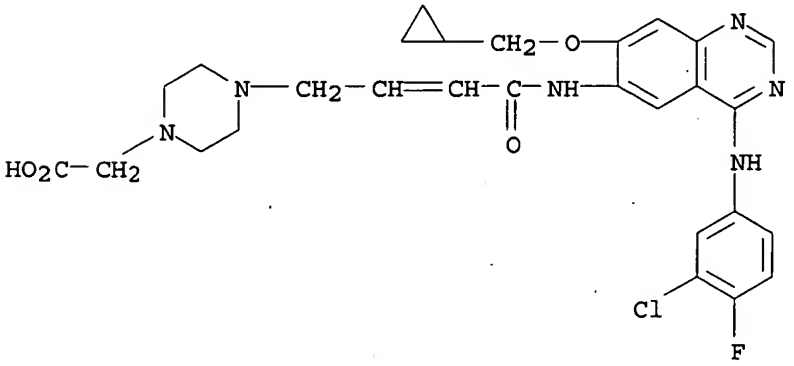
RN 290302-97-5 CAPLUS
CN Ethanethioic acid, S-[2-[[4-[[4-[(3-bromophenyl)amino]-7-methoxy-6-quinazolinyl]amino]-4-oxo-2-butenyl]methylamino]ethyl] ester (9CI) (CA INDEX NAME)



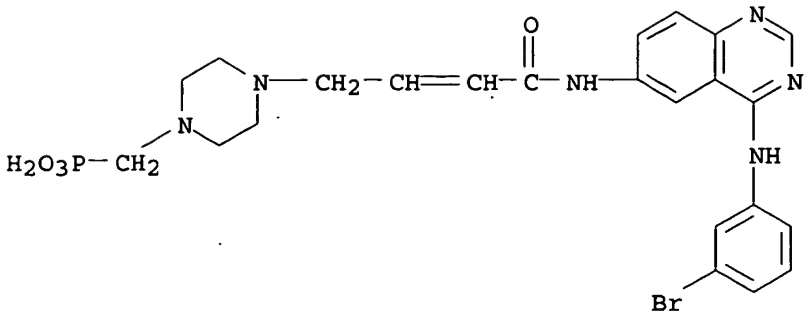
RN 290302-99-7 CAPLUS
CN .beta.-Alanine, N-[4-[[4-[(3-bromophenyl)amino]-7-methoxy-6-quinazolinyl]amino]-4-oxo-2-butenyl]-N-(carboxymethyl)- (9CI) (CA INDEX NAME)



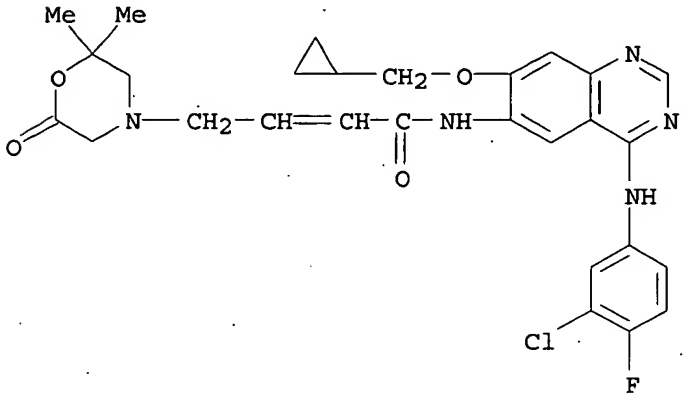
RN 290303-00-3 CAPLUS
CN 1-Piperazineacetic acid, 4-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]amino]-4-oxo-2-butenyl]- (9CI) (CA INDEX NAME)



RN 290303-01-4 CAPLUS
CN Phosphonic acid, [[4-[4-[[4-[(3-bromophenyl)amino]-6-quinazolinyl]amino]-4-oxo-2-butenyl]-1-piperazinyl]methyl]- (9CI) (CA INDEX NAME)

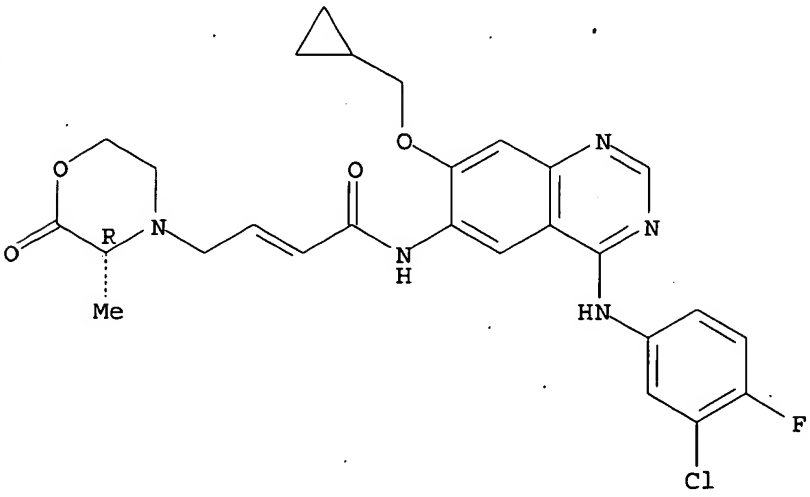


RN 290303-02-5 CAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-(2,2-dimethyl-6-oxo-4-morpholinyl)- (9CI) (CA INDEX NAME)

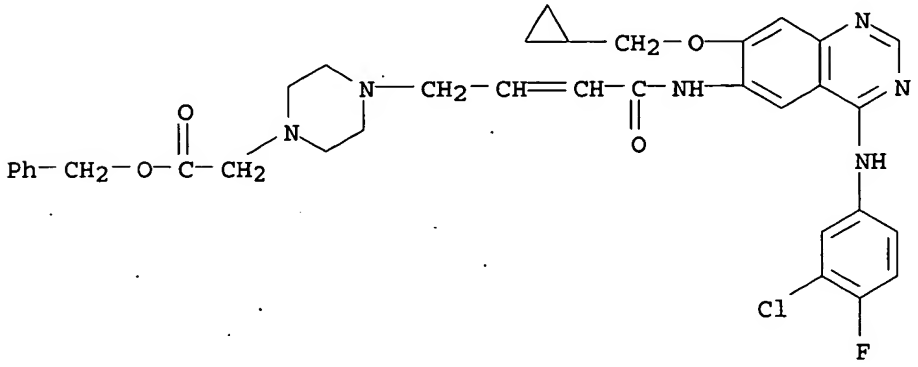


RN 290303-03-6 CAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-[(3R)-3-methyl-2-oxo-4-morpholinyl]- (9CI) (CA INDEX NAME)

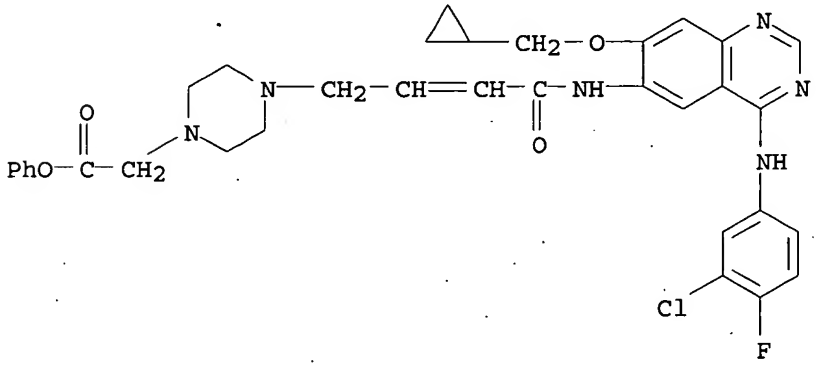
Absolute stereochemistry.
Double bond geometry unknown.



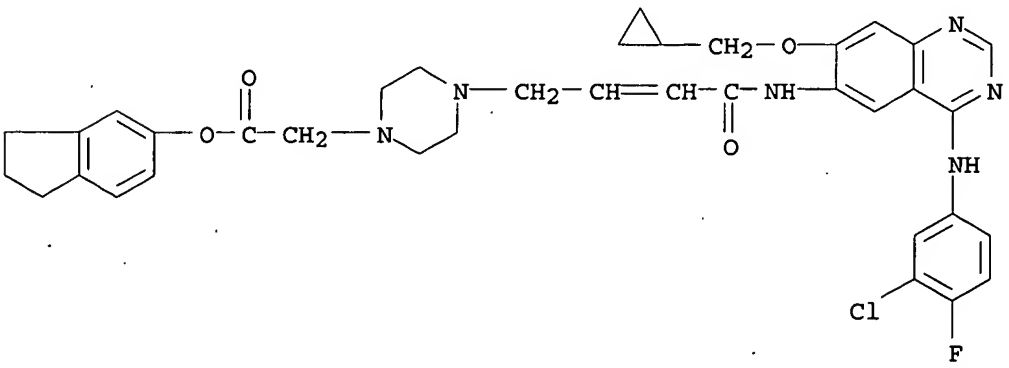
RN 290303-05-8 CAPLUS
CN 1-Piperazineacetic acid, 4-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]amino]-4-oxo-2-butenyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)



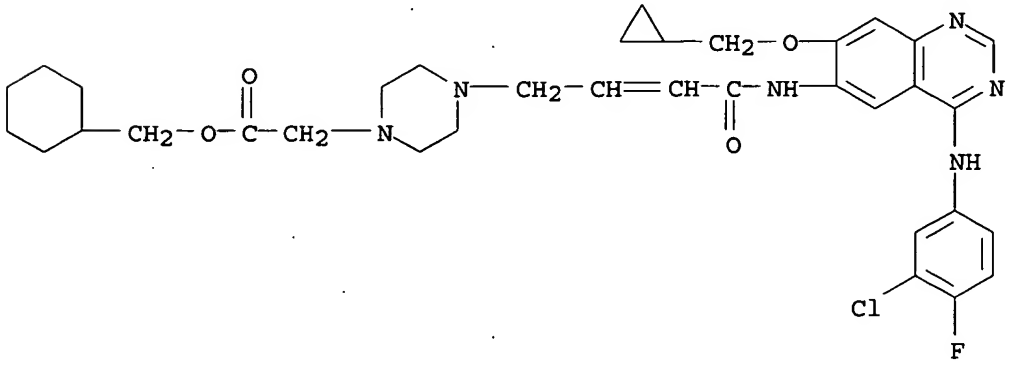
RN 290303-06-9 CAPLUS
CN 1-Piperazineacetic acid, 4-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]amino]-4-oxo-2-butenyl]-, phenyl ester (9CI) (CA INDEX NAME)



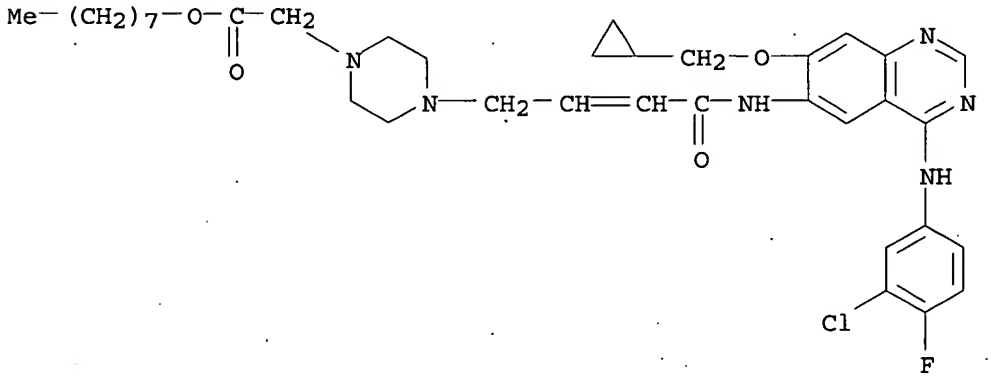
RN 290303-07-0 CAPLUS
CN 1-Piperazineacetic acid, 4-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]amino]-4-oxo-2-butenyl]-, 2,3-dihydro-1H-inden-5-yl ester (9CI) (CA INDEX NAME)



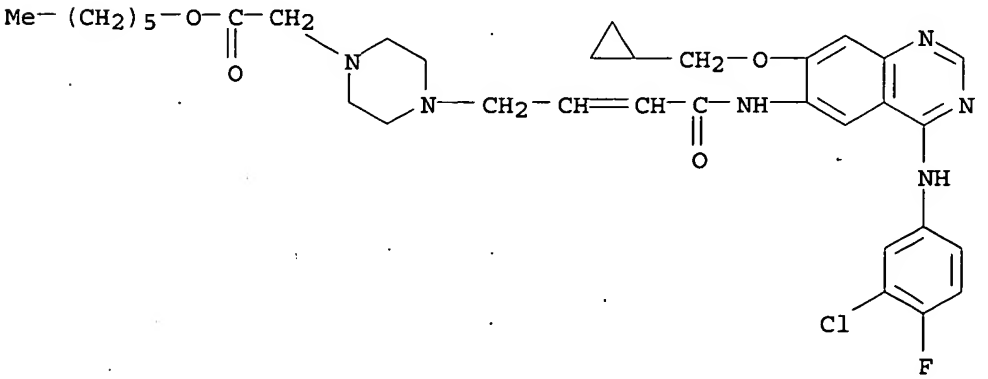
RN 290303-08-1 CAPLUS
CN 1-Piperazineacetic acid, 4-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]amino]-4-oxo-2-butenyl]-, cyclohexylmethyl ester (9CI) (CA INDEX NAME)



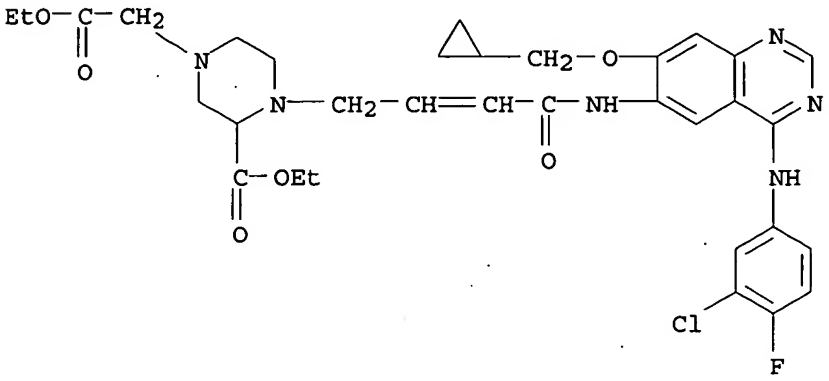
RN 290303-09-2 CAPLUS
CN 1-Piperazineacetic acid, 4-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]amino]-4-oxo-2-butenyl]-, octyl ester (9CI) (CA INDEX NAME)



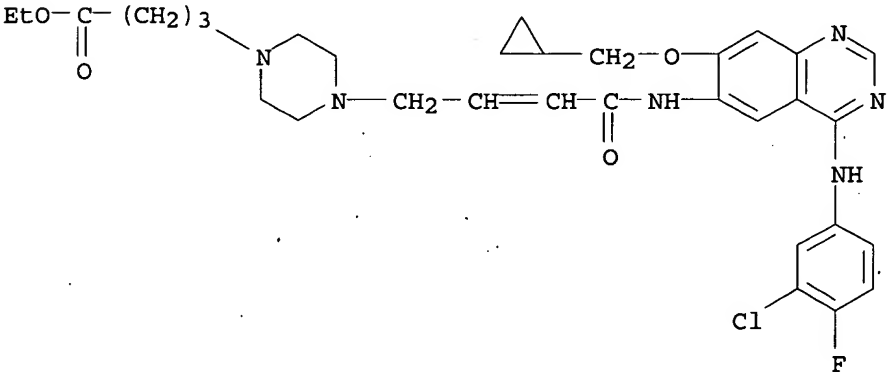
RN 290303-10-5 CAPLUS
CN 1-Piperazineacetic acid, 4-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]amino]-4-oxo-2-butenyl]-, hexyl ester (9CI) (CA INDEX NAME)



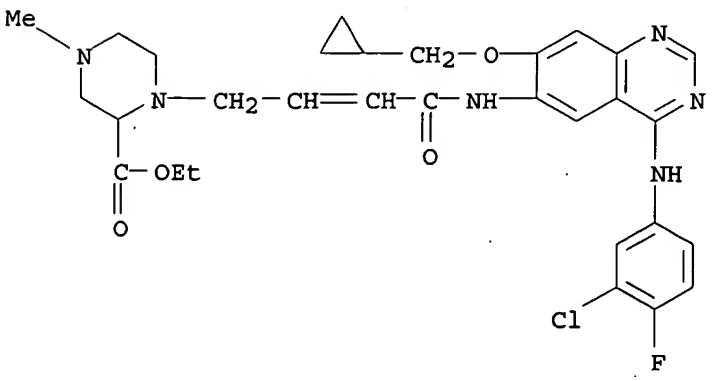
RN 290303-11-6 CAPLUS
CN 1-Piperazineacetic acid, 4-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]amino]-4-oxo-2-butenyl]-3-(ethoxycarbonyl)-, ethyl ester (9CI) (CA INDEX NAME)



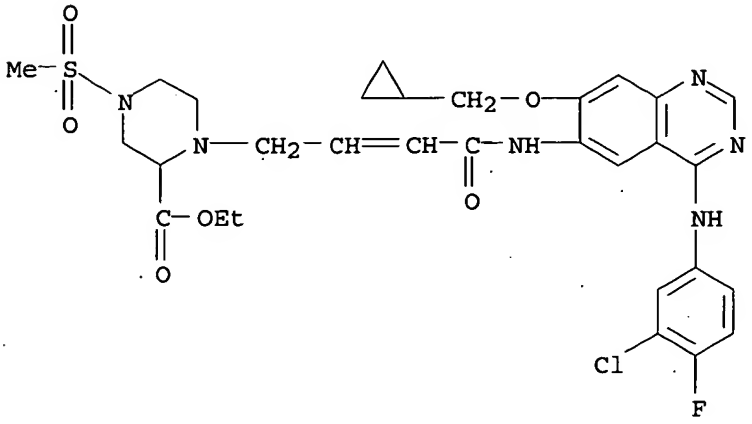
RN 290303-12-7 CAPLUS
CN 1-Piperazinebutanoic acid, 4-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]amino]-4-oxo-2-butenyl]-, ethyl ester (9CI) (CA INDEX NAME)



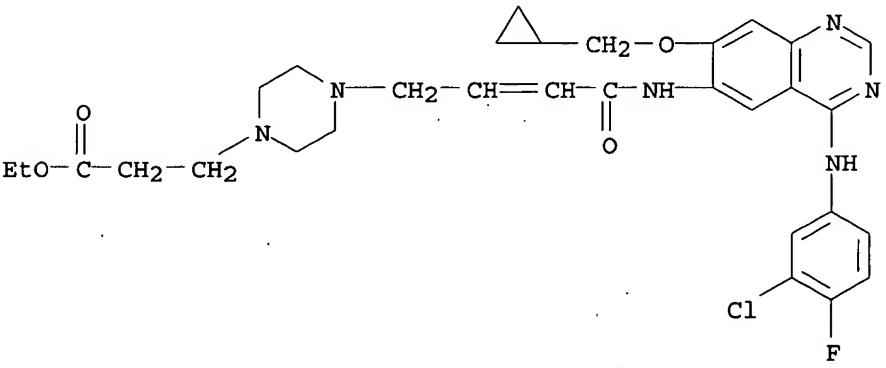
RN 290303-14-9 CAPLUS
CN 2-Piperazinecarboxylic acid, 1-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]amino]-4-oxo-2-butenyl]-4-methyl-, ethyl ester (9CI) (CA INDEX NAME)



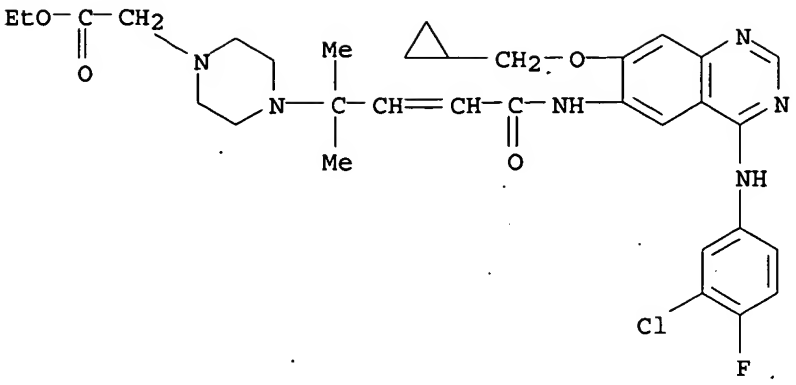
RN 290303-15-0 CAPLUS
CN 2-Piperazinecarboxylic acid, 1-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]amino]-4-oxo-2-butenyl]-4-(methylsulfonyl)-, ethyl ester (9CI) (CA INDEX NAME)



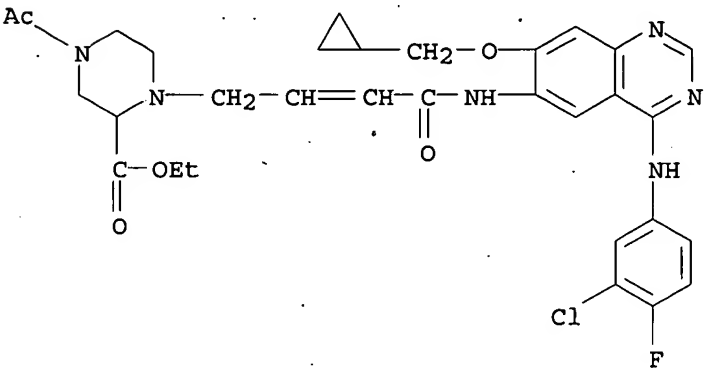
RN 290303-16-1 CAPLUS
CN 1-Piperazinepropanoic acid, 4-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]amino]-4-oxo-2-butenyl]-, ethyl ester (9CI) (CA INDEX NAME)



RN 290303-17-2 CAPLUS
CN 1-Piperazineacetic acid, 4-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]amino]-1,1-dimethyl-4-oxo-2-butenyl]-, ethyl ester (9CI) (CA INDEX NAME)



RN 290303-18-3 CAPLUS
CN 2-Piperazinecarboxylic acid, 4-acetyl-1-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]amino]-4-oxo-2-butenyl]-, ethyl ester (9CI) (CA INDEX NAME)



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 10 OF 13 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2000:607393 CAPLUS
DOCUMENT NUMBER: 133:207916
TITLE: Preparation of aminoquinazolines as epidermal growth factor receptor inhibitors.
INVENTOR(S): Himmelsbach, Frank; Langkopf, Elke; Jung, Birgit; Metz, Thomas
PATENT ASSIGNEE(S): Boehringer Ingelheim Pharma K-G, Germany
SOURCE: Ger. Offen., 26 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

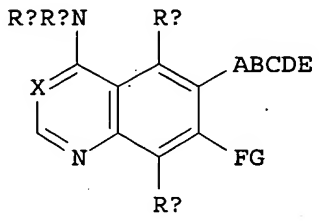
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 19908567	A1	20000831	DE 1999-19908567	19990227
CA 2361174	AA	20000908	CA 2000-2361174	20000224
WO 2000051991	A1	20000908	WO 2000-EP1496	20000224

W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA,

	MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI,				
	SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM,				
	AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW:	GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE,				
	DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF,				
	CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
NZ 513802	A	20010928	NZ 2000-513802	20000224	
EP 1157011	A1	20011128	EP 2000-910695	20000224	
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,				
	IE, SI, LT, LV, FI, RO				
BR 2000008524	A	20011218	BR 2000-8524	20000224	
JP 2002538145	T2	20021112	JP 2000-602218	20000224	
EE 200100449	A	20021216	EE 2001-449	20000224	
BG 105765	A	20020329	BG 2001-105765	20010801	
HR 20010617	A1	20021031	HR 2001-617	20010823	
NO 2001004114	A	20011015	NO 2001-4114	20010824	
PRIORITY APPLN. INFO.:			DE 1999-19908567 A	19990227	
			DE 1999-19911366 A	19990315	
			DE 1999-19928306 A	19990621	
			US 1999-149329P P	19990817	
			DE 1999-19954816 A	19991113	
			WO 2000-EP1496 W	20000224	

OTHER SOURCE(S): MARPAT 133:207916

GI



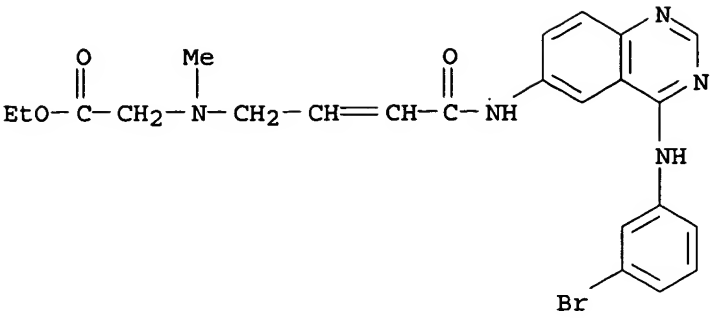
I

AB Title compds. [I; Ra = H, alkyl; Rb = (substituted) Ph, PhCH2, 1-phenylethyl; Rc, Rm = H, F, Cl, MeO, (methoxy-, dimethylamino-, diethylamino-, pyrrolidino-, piperidino-, morpholino- substituted) Me; X = N, NCC; A = O, alkylimino; B = CO, SO2; C = (Me- or F3C-substituted) allenylene, vinylene; D = (fluorinated) alkylene, carbonylalkylene, sulfonylalkylene, etc.; E, G = (substituted) R6O2CYNR5, etc.; R5 = H, (substituted) alkyl; R6 = H, (substituted) alkyl, cycloalkyl, alkenyl, alkynyl, etc.; F = alkylene, oxyalkylene, O; FG = H, F, Cl, alkoxy, etc.], were prepd. Thus, 6-amino-4-[(3-bromophenyl)amino]-7-[3-[4-(ethoxycarbonyl)methylpiperazin-1-yl]propoxy]quinazoline (prepn. given) in CH2Cl2 contg. Et3N was treated with acryloyl chloride in CH2Cl2 at -10.degree. to give 62% 4-[(3-bromophenyl)amino]-7-[3-[4-[(ethoxycarbonyl)methyl]piperazin-1-yl]propyloxy]-6-[(vinylcarbonyl)amino]quinazoline. The latter inhibited EGF-dependent proliferation with IC50 = 2.6 nM.

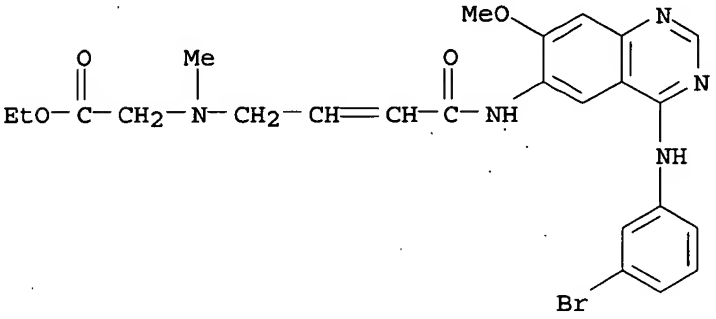
IT **289700-68-1P 289700-69-2P 289700-70-5P 289700-71-6P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of aminoquinazolines as epidermal growth factor receptor inhibitors)

RN 289700-68-1 CAPLUS

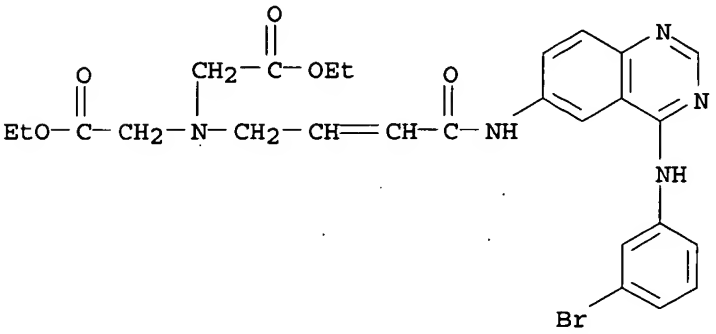
CN Glycine, N-[4-[[4-[(3-bromophenyl)amino]-6-quinazolinyl]amino]-4-oxo-2-butenyl]-N-methyl-, ethyl ester (9CI) (CA INDEX NAME)



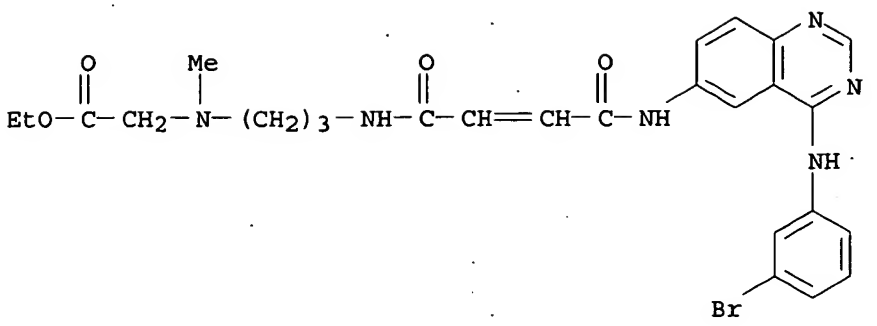
RN 289700-69-2 CAPLUS
CN Glycine, N-[4-[[4-[(3-bromophenyl)amino]-7-methoxy-6-quinazolinyl]amino]-4-oxo-2-butenyl]-N-methyl-, ethyl ester (9CI) (CA INDEX NAME)



RN 289700-70-5 CAPLUS
CN Glycine, N-[4-[[4-[(3-bromophenyl)amino]-6-quinazolinyl]amino]-4-oxo-2-butenyl]-N-(2-ethoxy-2-oxoethyl)-, ethyl ester (9CI) (CA INDEX NAME)



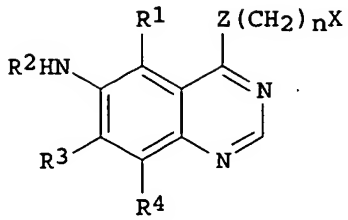
RN 289700-71-6 CAPLUS
CN Glycine, N-[3-[[4-[[4-[(3-bromophenyl)amino]-6-quinazolinyl]amino]-1,4-dioxo-2-butenyl]amino]propyl]-N-methyl-, ethyl ester (9CI) (CA INDEX NAME)



L3 ANSWER 11 OF 13 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1999:139833 CAPLUS
DOCUMENT NUMBER: 130:196664
TITLE: Preparation of 4-phenylaminoquinazolin-6-ylamides and related compounds as tyrosine kinase inhibitors.
INVENTOR(S): Wissner, Allan; Tsou, Hwei-ru; Johnson, Bernard Dean; Hamann, Philip Ross; Zhang, Nan
PATENT ASSIGNEE(S): American Cyanamid Company, USA
SOURCE: PCT Int. Appl., 121 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9909016	A1	19990225	WO 1998-US15789	19980729
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
TW 436485	B	20010528	TW 1998-87112356	19980728
AU 9886023	A1	19990308	AU 1998-86023	19980729
AU 757418	B2	20030220		
EP 1000039	A1	20000517	EP 1998-937275	19980729
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, SI, LT, LV, FI, RO				
BR 9811805	A	20000815	BR 1998-11805	19980729
US 6251912	B1	20010626	US 1998-124365	19980729
JP 2001515071	T2	20010918	JP 2000-509699	19980729
ZA 9806905	A	20000131	ZA 1998-6905	19980731
NO 2000000487	A	20000331	NO 2000-487	20000131

PRIORITY APPLN. INFO.: US 1997-904942 A 19970801
US 1997-55072P P 19970801
WO 1998-US15789 W 19980729
OTHER SOURCE(S): MARPAT 130:196664
GI



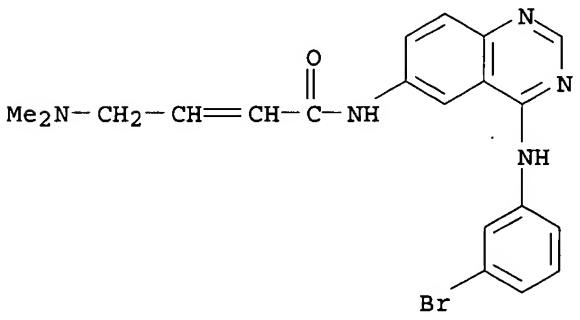
I

AB Title compds. [I; X = (substituted) cycloalkyl, pyridinyl, pyrimidinyl, Ph; Z = NH, O, S, NR; R = alkyl; R1, R3, R4 = H, halo, alkyl, alkenyl, alkynyl, alkenyloxy, alkynyloxy, CH2OH, halomethyl, alkanoyloxy, alkenoyloxy, alkynoyloxy, alkanoyloxymethyl, etc.; R2 = R5C.tplbond.CCO, (R5)2C:CR5CO, R5SS[C(R5)2]rCO, etc.; n = 0, 1; r = 1-4; R5 = H, CO2H, carboalkoxy, Ph, etc.], were prepd. Thus, 4-dimethylamino-2-butynoic acid (prepn. given) was stirred with iso-Bu chloroformate and N-methylmorpholine in THF with ice cooling; N-(3-bromophenyl)-4,6-quinazolinediamine in pyridine was added and the mixt. was stirred 2 h at 0.degree. to give 4-dimethylamino-2-butynoic acid [4-(3-bromophenylamino)quinazolin-6-yl]amide. The latter inhibited MB435 tumor cell growth with IC50 = 0.05 .mu.g/mL.

IT **220699-51-4P 220699-67-2P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of 4-phenylaminoquinazolin-6-ylamides and related compds. as tyrosine kinase inhibitors)

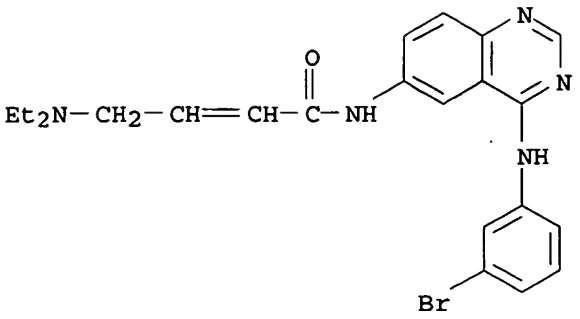
RN 220699-51-4 CAPLUS

CN 2-Butenamide, N-[4-[(3-bromophenyl)amino]-6-quinazolinyl]-4-(dimethylamino)- (9CI) (CA INDEX NAME)



RN 220699-67-2 CAPLUS

CN 2-Butenamide, N-[4-[(3-bromophenyl)amino]-6-quinazolinyl]-4-(diethylamino)- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 12 OF 13 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1999:113656 CAPLUS
DOCUMENT NUMBER: 130:168387
TITLE: Irreversible inhibitors of tyrosine kinases
INVENTOR(S): Bridges, Alexander James
PATENT ASSIGNEE(S): Warner-Lambert Company, USA
SOURCE: PCT Int. Appl., 124 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9906378	A1	19990211	WO 1998-US15784	19980729
W: AL, AU, BA, BB, BG, BR, CA, CN, CZ, EE, GE, HR, HU, ID, IL, IS, JP, KR, LC, LK, LR, LT, LV, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, SL, TR, TT, UA, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9887607	A1	19990222	AU 1998-87607	19980729
US 6127374	A	20001003	US 1999-269545	19990325
US 6562818	B1	20030513	US 2000-593031	20000613

PRIORITY APPLN. INFO.: US 1997-54060P P 19970729
WO 1998-US15784 W 19980729
US 1999-269545 A3 19990325
OTHER SOURCE(S): MARPAT 130:168387

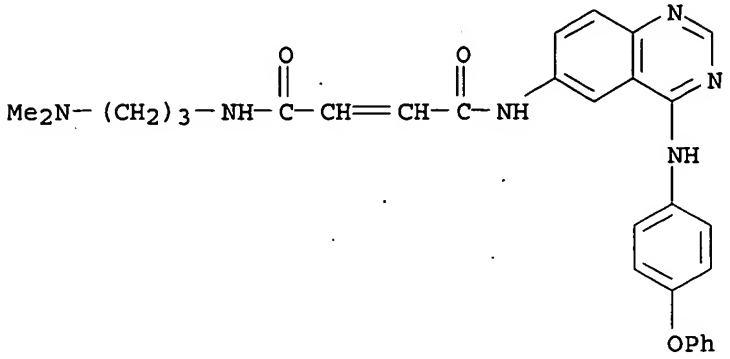
AB Pyrimidine derivs. that are irreversible inhibitors of tyrosine kinases are reported. Thus, PhCH2OH was treated with 4-FC6H4NO2 to give 4-PhCH2OC6H4NO2, which was reduced to the amine and used to aminate 4-chloro-6-nitroquinazoline hydrochloride. The resulting 6-nitro-4-(4-benzyloxyanilino)quinazoline hydrochloride was reduced to the amine and acylated to give N-[4-(4-benzyloxyanilino)quinazolin-6-yl]acrylamide (I). I had an IC50 for inhibition of epidermal growth factor receptor tyrosine kinase of 3.6 nM.

IT **220488-58-4P 220488-59-5P 220488-62-0P 220488-63-1P 220489-99-6P 220490-00-6P 220490-03-9P 220490-04-0P**
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of anilinoquinazolinylacrylamides and related compds. as tyrosine kinase inhibitors)

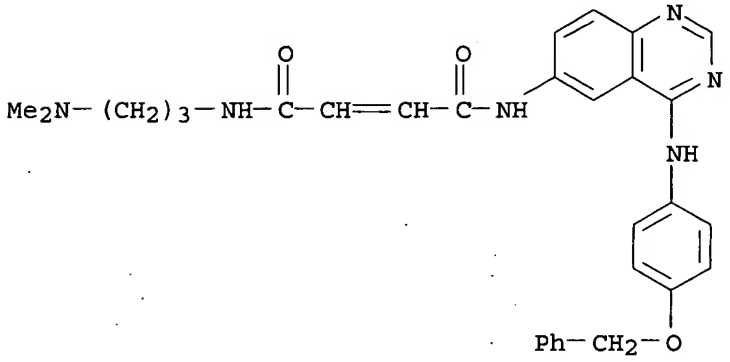
RN 220488-58-4 CAPLUS

10/ 023,099

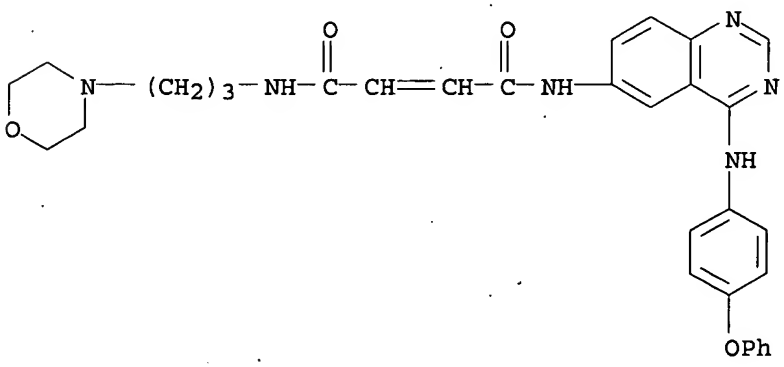
CN 2-Butenediamide, N-[3-(dimethylamino)propyl]-N'-[4-[(4-phenoxyphenyl)amino]-6-quinazolinyl]- (9CI) (CA INDEX NAME)



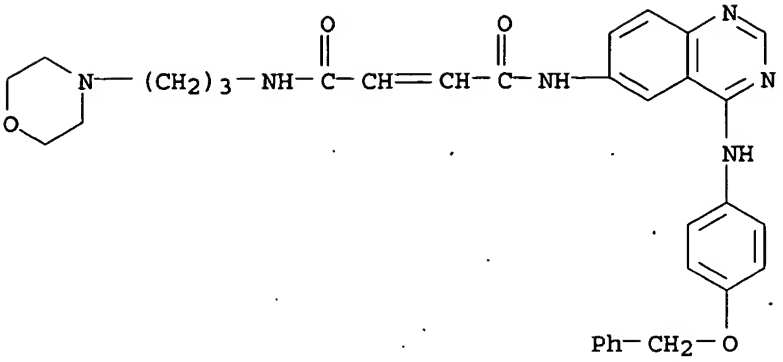
RN 220488-59-5 CAPLUS
CN 2-Butenediamide, N-[3-(dimethylamino)propyl]-N'-[4-[[4-(phenylmethoxy)phenyl]amino]-6-quinazolinyl]- (9CI) (CA INDEX NAME)



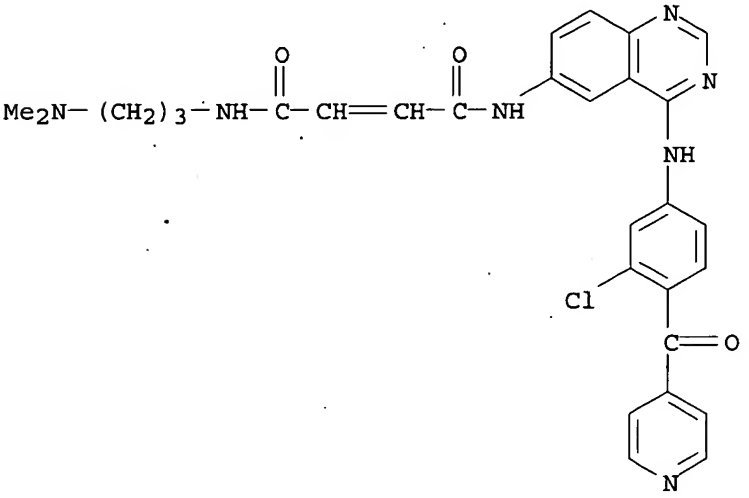
RN 220488-62-0 CAPLUS
CN 2-Butenediamide, N-[3-(4-morpholinyl)propyl]-N'-[4-[(4-phenoxyphenyl)amino]-6-quinazolinyl]- (9CI) (CA INDEX NAME)



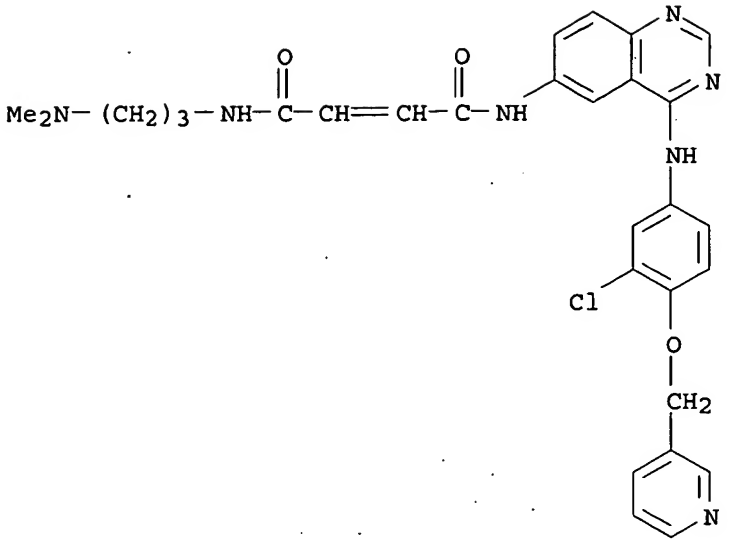
RN 220488-63-1 CAPLUS
CN 2-Butenediamide, N-[3-(4-morpholinyl)propyl]-N'-[4-[[4-(phenylmethoxy)phenyl]amino]-6-quinazolinyl]- (9CI) (CA INDEX NAME)



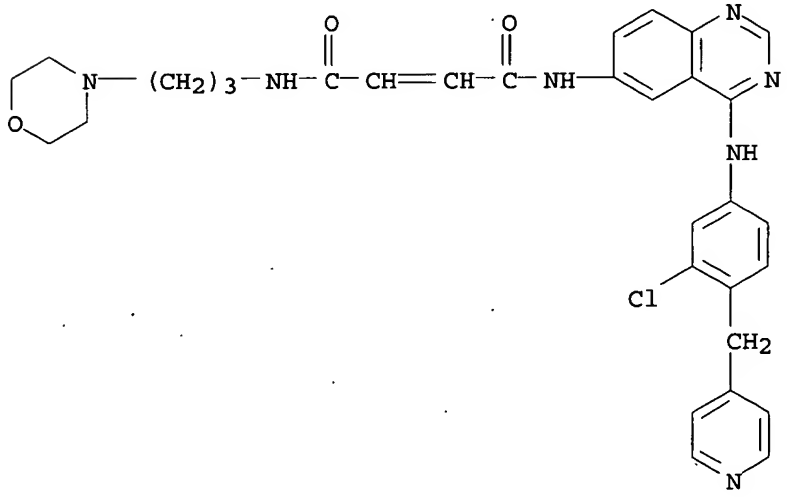
RN 220489-99-6 CAPLUS
CN 2-Butenediamide, N-[4-[[3-chloro-4-(4-pyridinylcarbonyl)phenyl]amino]-6-quinazolinyl]-N'-[3-(dimethylamino)propyl]- (9CI) (CA INDEX NAME)



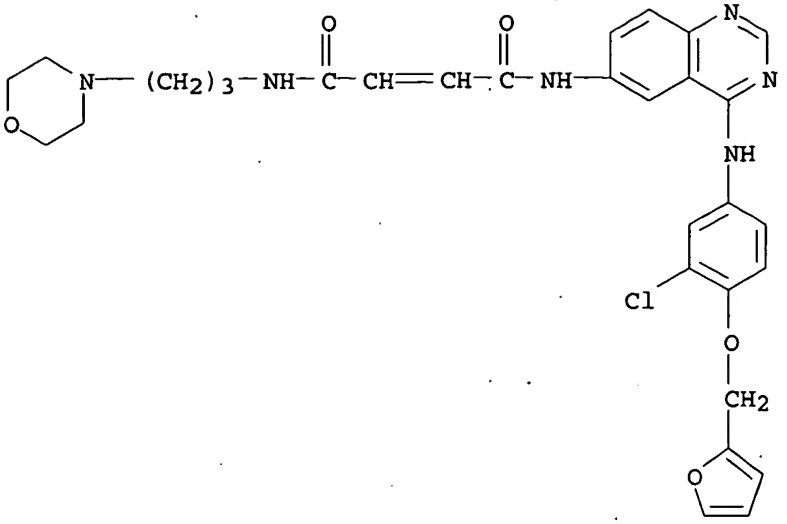
RN 220490-00-6 CAPLUS
CN 2-Butenediamide, N-[4-[[3-chloro-4-(3-pyridinylmethoxy)phenyl]amino]-6-quinazolinyl]-N'-[3-(dimethylamino)propyl]- (9CI) (CA INDEX NAME)



RN 220490-03-9 CAPLUS
CN 2-Butenediamide, N-[4-[[3-chloro-4-(4-pyridinylmethyl)phenyl]amino]-6-quinazolinyl]-N'-[3-(4-morpholinyl)propyl]- (9CI) (CA INDEX NAME)



RN 220490-04-0 CAPLUS
CN 2-Butenediamide, N-[4-[[3-chloro-4-(2-furanylmethoxy)phenyl]amino]-6-quinazolinyl]-N'-[3-(4-morpholinyl)propyl]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 13 OF 13 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1997:696745 CAPLUS
DOCUMENT NUMBER: 128:3695
TITLE: Preparation of N-quinazolinylacrylamides and analogs as tyrosine kinase inhibitors
INVENTOR(S): Bridges, Alexander James; Denny, William Alexander; Dobrusin, Ellen Myra; Doherty, Annette Marian; Fry, David W.; Mcnamara, Dennis Joseph; Showalter, Howard Daniel Hollis; Smaill, Jeffrey B.; Zhou, Hairong; et al.
PATENT ASSIGNEE(S): Warner-Lambert Company, USA; Bridges, Alexander James; Denny, William Alexander; Dobrusin, Ellen Myra; Doherty, Annette Marian; Fry, David W.; Mcnamara, Dennis Joseph; Showalter, Howard Daniel Hollis; Smaill, Jeffrey B.; Zhou, Hairong
SOURCE: PCT Int. Appl., 193 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9738983	A1	19971023	WO 1997-US5778	19970408
W: AL, AU, BA, BB, BG, BR, CA, CN, CZ, EE, GE, GH, HU, IL, IS, JP, KR, LC, LK, LR, LT, LV, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, TR, TT, UA, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2249446	AA	19971023	CA 1997-2249446	19970408
AU 9724463	A1	19971107	AU 1997-24463	19970408
AU 725533	B2	20001012		
EP 892789	A1	19990127	EP 1997-920213	19970408
EP 892789	B1	20020227		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI				

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CN 1218456	A	19990602	CN 1997-194458		19970408
BR 9708640	A	19990803	BR 1997-8640		19970408
JP 2000508657	T2	20000711	JP 1997-537173		19970408
JP 3370340	B2	20030127			
AT 213730	E	20020315	AT 1997-920213		19970408
ES 2174250	T3	20021101	ES 1997-920213		19970408
ZA 9703060	A	19971104	ZA 1997-3060		19970410
BG 63160	B1	20010531	BG 1998-102811		19981001
NO 9804718	A	19981209	NO 1998-4718		19981009
KR 2000005364	A	20000125	KR 1998-708086		19981010
US 6344459	B1	20020205	US 1999-155501		19990608
PRIORITY APPLN. INFO.:			US 1996-15351P	P	19960412
			WO 1997-US5778	W	19970408

OTHER SOURCE(S): MARPAT 128:3695

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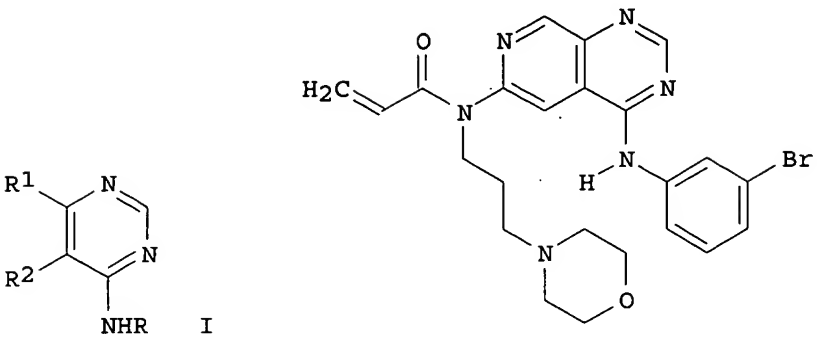


I II

AB Title compds. [I; R = (CHR6)pR9; R1R2 = CH:CR7CR8:CH, CH:CR7CR8:N, CH:CR7N:CH, etc.; R6 = H or alkyl; 1 of R7,R8 = Z1Z2R10 and the other = OR4, SR4, NHR3; R3,R4 = (un)substituted alkyl, heterocyclylalkyl, etc.; R9 = (un)substituted Ph; R10 = CR11:CHR5, C.tplbond.CR5, CR11:C:CHR5; R5 = H, halo, alkyl, Ph, etc.; R11 = H, halo, alkyl; Z1 = bond, O, (alkyl)imino, CH2, etc.; Z2 = CO, SO, P(O)(OH), etc.; p = 0 or 1] were prepd. Thus, I (R = C6H4Br-3, R1R2 = CH:NCR8:CH, R8 = F) was condensed with 3-morpholinoprpanamine and the product acylated by CH2:CHCOCl to give title compd. II. Data for biol. activity of I were given.

IT **198960-34-8P 198960-63-3P 198960-87-1P**
198961-22-7P 198961-42-1P 198961-43-2P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of N-quinazolinylacrylamides and analogs as tyrosine kinase inhibitors)

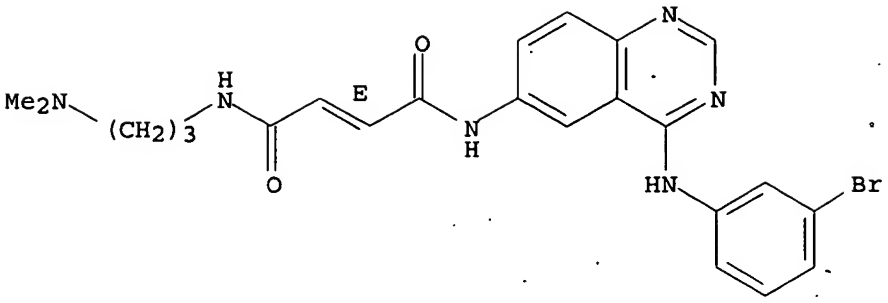
RN 198960-34-8 CAPLUS

CN 2-Butenediamide, N-[4-[(3-bromophenyl)amino]-6-quinazolinyl]-N'-[3-(dimethylamino)propyl]-, (2E)-, tris(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

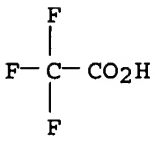
CRN 198960-33-7
CMF C23 H25 Br N6 O2

Double bond geometry as shown.

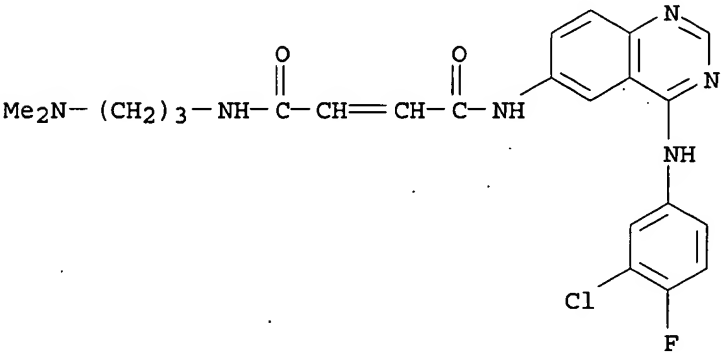


CM 2

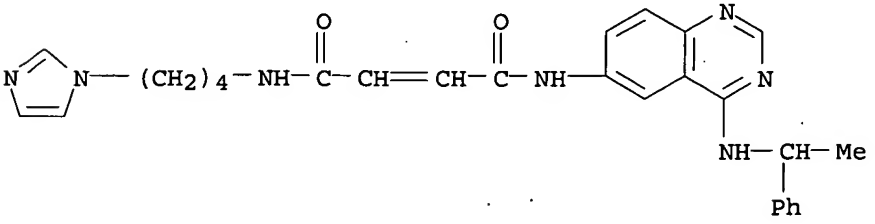
CRN 76-05-1
CMF C2 H F3 O2



RN 198960-63-3 CAPLUS
CN 2-Butenediamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-6-quinazolinyl]-N'-[3-(dimethylamino)propyl]- (9CI) (CA INDEX NAME)



RN 198960-87-1 CAPLUS
CN 2-Butenediamide, N-[4-(1H-imidazol-1-yl)butyl]-N'-[4-[(1-phenylethyl)amino]-6-quinazolinyl]- (9CI) (CA INDEX NAME)



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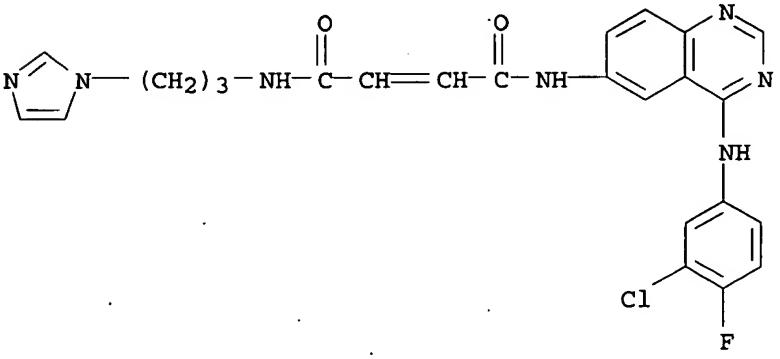
RN 198961-22-7 CAPLUS
CN 2-Butenediamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-6-quinazolinyl]-N'-[3-(1H-imidazol-1-yl)propyl]- (9CI) (CA INDEX NAME)



RN 198961-42-1 CAPLUS
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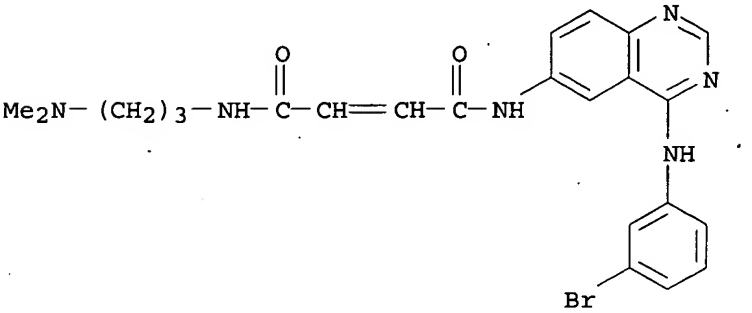
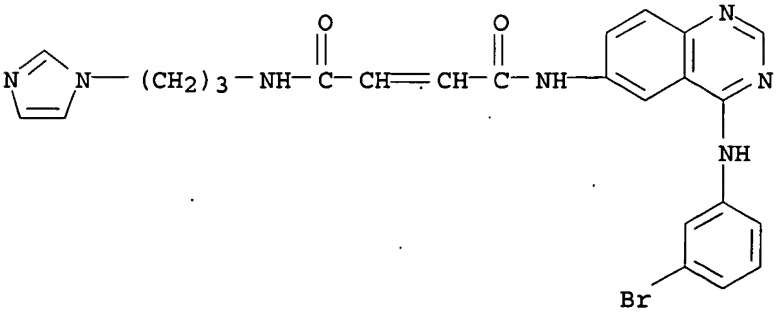


RN 198961-43-2 CAPLUS
CN 2-Butenediamide, N-[4-[(3-bromophenyl)amino]-6-quinazolinyl]-N'-[3-(1H-imidazol-1-yl)propyl]- (9CI) (CA INDEX NAME)



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L3 13 S L2

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COST IN U.S. DOLLARS

	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	60.64	209.00

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)

	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-8.46	-8.46

STN INTERNATIONAL LOGOFF AT 13:10:37 ON 01 JUL 2003